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THE MEDICAL CLINICS
OF
NORTH AMERICA

VOLUME 1 NUMBER 4

CLINIC OF DR. HENRY A. CHRISTIAN

PETER BENT BRIGHAM HOSPITAL, BOSTON

COMPLETE HEART-BLOCK

October 8, 1917.

DR. CHRISTIAN (to a student): Please feel that patient's pulse (P. B. B. H., Med. No. 7345), and as you feel it describe what you make out.

STUDENT: It is very slow.

DR. CHRISTIAN: In the first place, it is a very slow pulse. It has been running about 35 or 36.

STUDENT: It seems to be quite regular.

DR. CHRISTIAN: Yes, it is regular. What are the other characteristics of the pulse? You have given the rate and the rhythm.

STUDENT: There is high tension.

DR. CHRISTIAN: Yes, the tension is high. What about the volume of the pulse?

STUDENT: It is rather increased in volume, I should say.

DR. CHRISTIAN: What other characteristics do you look for in examining a pulse besides what you have already mentioned?

STUDENT: Examine the artery.

DR. CHRISTIAN: What about the artery?

STUDENT: The artery is thickened.

DR. CHRISTIAN: How can you tell whether what you feel is due to the volume and tension of the pulse or thickening of the vessel wall?

STUDENT: You feel the artery after you have stopped the pulse by the finger.

DR. CHRISTIAN: See how that works.

STUDENT: The radial seems thickened.

DR. CHRISTIAN: The pulse is one of good volume and the vessel wall, in addition, is thickened. Look at his brachial arteries to see if you get any information from those in regard to the condition of the artery wall. We are dealing with a patient with a very slow regular pulse, a pulse of good volume, and the artery has a thickened wall.

STUDENT: There is very definite thickening of the wall in the brachial. It is evident there that the pulsation is very marked.

DR. CHRISTIAN: What would you say about that type of pulsation in the brachial? You see there is quite an unusually prominent pulsation in the brachial vessels. What would you say about it? What kind of pulsation is that?

STUDENT: It is not very strong. It comes sharply and then disappears altogether.

DR. CHRISTIAN: Yes, and what else? What is the direction of the pulsation?

STUDENT: Down the artery.

DR. CHRISTIAN: Do you say that because you see it or because you think that is the way it ought to go?

STUDENT: It seems to me I see it first here above and then here below.

DR. CHRISTIAN: Well, that may be true. You may have keen eyesight. The pulse-wave travels very fast and is not an obvious thing. What else?

STUDENT: It is tortuous.

DR. CHRISTIAN: Yes, the artery is tortuous, and what about the pulsation? That is a lateral pulsation. The vessel moves to the side instead of merely heaving, as you would expect. In addition to the lifting pulsation there is a distinctly lateral pulsation—sometimes in one direction, sometimes in the other. Why is that?

STUDENT: It is due to the pressure of the blood in the artery and difficulty of the blood in passing through the arterioles.

DR. CHRISTIAN: That causes high pressure. Why is that vessel tortuous?

STUDENT: It is due to arteriosclerosis.

DR. CHRISTIAN: I mean in a physical sense. Why has it become tortuous?

STUDENT: It has been forced by the pressure—the difficulty of the blood in passing through the arterioles causes back-pressure through the artery.

DR. CHRISTIAN: Does back-pressure usually bend the artery? The blood-pressure is 220 systolic and 60 diastolic, so that it is high. The tortuosity means that the vessel has lengthened. Of course, pressure has a part in that, but perfectly normal pressure may cause the vessel to lengthen. The vessel is relatively fixed at the two ends and if it lengthens it becomes tortuous. The vessel wall dilates or the vessel wall lengthens, or it may both dilate and lengthen. These changes indicate disturbances in the vessel wall. If it dilates irregularly as you run your fingers over it you feel irregularities in the bore of the vessel. If it lengthens, but does not dilate or thicken, you simply see this lateral pulsation, indicating a tortuous artery. The way to recognize the fact that the vessel has lengthened is to watch the pulsation and see if there is a lateral pulsation or to feel the vessel to see if it has become tortuous. This artery looks almost like a worm moving under the skin, particularly in the small branches of the vessel where the curve shifts to one side and then shifts in the other direction.

DR. CHRISTIAN: How does the vessel feel? Is it uniform in size or is it unevenly dilated in different degrees at different places?

STUDENT: It is uniform.

DR. CHRISTIAN: I do not think so. If you run your finger up and down that vessel you feel distinctly narrower and wider places. What do those phenomena teach you about the structure of the vessel wall?

STUDENT: The vessel wall is thickened and hardened.

DR. CHRISTIAN: Why do you say "hardened"?

STUDENT: I can feel that it is hardened—it feels hard under my finger.

DR. CHRISTIAN: Is that due to the thickening—change in the vessel wall—or is it due to the pressure? You can tell that by blotting out the current and seeing what sensation you get without the pulsation.

STUDENT: I should say that there was still some hardening.

DR. CHRISTIAN: I should say that the vessel wall is thick, but it is not a particularly hard vessel. We see calcified vessels that are very firm under your finger, and feel hard like a pencil. As this artery is thickened irregularly you feel irregularities. It is a nodular vessel, but it is not a particularly hardened vessel. It is a sclerotic process and the arteriosclerosis has led to elongation of the vessel, and has led to irregular dilatation of the vessel and the various phenomena that were described. In addition, it is a case of high blood-pressure, so we have, in addition to all the other factors, this increased tension.

DR. CHRISTIAN: Let us look at his neck and see what we can see there.

STUDENT: There is the carotid pulse.

DR. CHRISTIAN: He is a sort of anomalous individual if the carotid is out there. (Discussion in locating the carotid pulse.) Put your fingers on the pulsation and see what you feel.

STUDENT: A very strong pulsation.

DR. CHRISTIAN: I do not feel anything at all there.

STUDENT: I pressed down on it.

DR. CHRISTIAN: I did not tell you to do that. I told you to put your fingers where you saw the pulsation; not to press in deeply. If you feel up here you get a very definite palpable pulse. If you feel down here under the upper edge of the bone there you get a pulsation. That is arterial, but in between where you see those pulsations, if you feel lightly, you get very little pulsation. If you go in deeper, feeling over the artery, you do get a pulsation, but the superficial pulsation is the one you see mostly and is the one you can blot out, but if you make deep pressure you can feel the artery underneath. A pulsation that you can see that way but do not feel much of is always a venous

pulse. It is visible, but not necessarily palpable. What is the rate of that pulsation as contrasted to the impulse at the apex or in the radial artery?

STUDENT: It is very much more rapid.

DR. CHRISTIAN: See if you can make out how many beats take place there compared with each one at the wrist.

STUDENT: There are three to each one in the wrist.

DR. CHRISTIAN: How many ought there to be to each one in the wrist?

STUDENT: One, but it ought not to be visible.

DR. CHRISTIAN: It is visible in a large number of people, and when it is visible how many ought there to be?

STUDENT: One.

DR. CHRISTIAN: What is that due to?

STUDENT: It is due to regurgitation in the veins during auricular systole.

DR. CHRISTIAN: Does not the ventricle produce any change in the veins?

STUDENT: No normal change.

DR. CHRISTIAN: Yes it does. Did not I draw on the board a few days ago a picture of the venous pulse? Did it not have more than one wave to it? How many waves did it have?

STUDENT: Three.

DR. CHRISTIAN: It had three waves—the "A" wave, the "C" wave, and the "V" wave. Ordinarily you cannot see with the cardiac cycle three waves, but if a pulse is going slowly you ought to see two pulsations in the jugular to one pulsation in the radial. One of those is probably the "A" wave and the other one is the "C" wave. Sometimes we can see all three. There is nothing particularly abnormal in seeing two pulsations in the jugular to one pulsation that you feel at the wrist. Very often when we have cardiac cases with decompensation and markedly distended jugular veins with a pretty rapid heart rate there are very numerous beats that you can see in the jugular, but they do not really exceed in number what is the normal relation. It is pretty hard by observation in these cases to say whether there are two or three that you see in the jugular while following the radial pulse, but

certainly there is more than one. Here is a patient with a very slow pulse, and as you watch there I think you can make out that there are distinctly about three visible pulsations in the neck to every one that you can feel, and then as you feel the pulse I think you can see that with the pulse-beat one of those waves is considerably more prominent than the other, and when that takes place all of his neck tissue raises up here, and that is the time of the carotid pulse, corresponding to what you feel, and in the interval between these more prominent pulsations you see a succession of small waves, and there are about two between these bigger ones, so there are really about three pulsations in the neck to one that you feel in the wrist.

DR. CHRISTIAN: Look at his cardiac region now and tell us what you see there in the way of pulsations.

STUDENT: There is a marked apex-beat from here to here. (Indicates on patient.)

DR. CHRISTIAN: Is that synchronous with what you feel at his wrist?

STUDENT: Yes.

DR. CHRISTIAN: When you feel the pulse at the wrist—the pulse-wave coming up—what happens to the apex? Does it go down or up? Is it a forward motion or is it a retraction?

STUDENT: It seems to me I feel the pulsation at the wrist just after the apex goes up.

DR. CHRISTIAN: Perhaps two things happen. Look right here at this particular point.

STUDENT: There seems to be a second little vibration after the first one.

DR. CHRISTIAN: Yes, that is true; there is a localized heave in the apex region when in these two spaces near the apex there is a retraction taking place. The chest seems to come up and then go in almost simultaneously. Then if you will feel in this place you will find that that is apex-beat, while what you described as apex-beat is rather a diffuse systolic retraction. There is a small area which just about the time that you feel the pulse in the wrist distinctly shoves up, and that is the apex-impulse. The adjacent tissue up over the precordium when the apex goes up retracts so

that you get a rather diffuse systolic retraction when at the apex there is a definite apex-impulse and apex-thrust. When the heart is going so slowly you can analyze those things. Of course, in normal cases with a normal rate you cannot analyze those things so well because the heart is beating too fast and the motion in the chest wall is slight. This is a good case in which to study the ordinary phenomena of the normal, just like experimentally slowing down the heart to analyze its parts. That heart is slowed down to 35 or 36 so you can see what is going on. There is very distinctly a thrust or impulse over rather a small apex region, and over all the adjacent precordium there is distinctly a systolic retraction. What causes that difference in those areas?

STUDENT: You mean the difference between the retraction and the thrust?

DR. CHRISTIAN: Yes; the things that we have seen.

STUDENT: The apex being thrust out pulls in the other part of the heart.

DR. CHRISTIAN: What part of the heart is that in the area where the retraction is?

STUDENT: There was retraction over the lower part of the right ventricle and below the heart.

DR. CHRISTIAN: That is not below the heart because the heart is out. The heart is enlarged. It comes out as far as we saw the apex. Put a little diagram of the anterior surface of the heart on the board and mark out what in the lower part is right ventricle and what is left ventricle. (Diagram made.) Probably more than you have put down is left ventricle. The amount of left ventricle that comes to the anterior surface varies a good deal in normal people, and when you come to hearts that have been enlarged usually a larger amount of left ventricle comes forward against the chest wall than takes place in normal hearts. In this patient with an enlarged heart probably in the apex region the left ventricle comes forward to a larger extent. Of course, we cannot tell just how much unless we had the heart in our hands, but a good deal more than normal and a very considerable amount probably is left ventricle. When the heart contracts of course the ventricle contracts and squeezes down, squeezing the blood

out, and that retraction is in large part due to the fact that the right ventricle has contracted, and as it contracts it pulls away from the chest wall. The apex-beat is made by the hardening of the tip of the heart, in this particular case probably in large part left ventricle, at the contraction, and in view of the fact that with the contraction there is a little rotation on the axis of the heart, so the heart as it contracts pushes a little forward and out. The ordinary apex-impulse is due to a combination of the contraction of the ventricle, hardening of the muscle, and with the contraction a slight rotation on the axis of the heart, so that the apex turns forward and outward, and in this particular case you can really see that and feel it unusually well because you can feel the powerfully contracted left ventricle as it turns itself out, as I said, in an area about the size of a five-cent piece, and then you can feel and see the retraction of the right ventricle. The right ventricle is markedly thinner than the left one. The whole thing is the contraction—the powerful muscle of the left ventricle hardening in contraction, then thrusting forward, and then the right ventricle with its thinner wall contracting, and the retraction is due more to the emptying of the right ventricle than to any palpable change in the character of the muscle, and that is exactly what you would expect if you had a thinner and a thicker layer of muscle and those layers of muscle contracting together. You also described a little secondary wave that you can see. It is a retraction which comes down and then goes back, so there is a little double wave that you can distinctly see in the retraction—you see an impulse and see a retraction. There is a rebound, so to speak, of the chest wall—it falls in and then comes out, and when it comes out it does not stop there; there is a rebound, so there is a double wave—the first one more marked, the second one slighter. Look to see if there is anything else.

STUDENT: Up in here there is a pulsation to the left of the sternal margin.

DR. CHRISTIAN: What way does that go in contrast to the other?

STUDENT: It seems to go in this way (indicating a downward direction).

DR. CHRISTIAN: I do not mean so much its transmission. When this is retracting, is that going forward or not?

STUDENT: I think it is. Yes, when this goes down, that goes up.

DR. CHRISTIAN: Yes, that is true. Over the upper part of the chest at the left of the sternum there is a pulsation which is just in the opposite direction to that at the apex. There is a sort of seesaw, when this goes down that comes up, and vice versa. What is that upper retraction due to?

STUDENT: That is from the aorta.

DR. CHRISTIAN: Where is the aorta here?

STUDENT: Along there to the left of the sternum.

DR. CHRISTIAN: That is all right as far as right and left is concerned. How about the anteroposterior direction?

STUDENT: It goes back.

DR. CHRISTIAN: Yes, the aorta is nearer the back than it is the front on the left side. The aorta is way back against the vertebral column, so I guess you do not see any aorta pulsating on the left side. The only point at which the aorta comes near the surface is here in the right chest just above the so-called aortic area. After that the curve goes rapidly posteriorly and to the left. What vessel does lie under the surface here on the left?

STUDENT: The pulmonary artery.

DR. CHRISTIAN: Yes, the pulmonary artery comes out and the aorta curves back in the posterior part of the chest. What else lies in this region?

STUDENT: Vessels.

DR. CHRISTIAN: Yes, vessels and parts of the heart.

STUDENT: Left auricle.

DR. CHRISTIAN: How much of the left auricle?

STUDENT: The left auricle goes back.

DR. CHRISTIAN: Most of the left auricle is behind. Does any come forward?

STUDENT: Just the tip.

DR. CHRISTIAN: Where does that come forward as far as the anterior surface of the chest is concerned or as far as the pulmonary artery is concerned?

STUDENT: Just below the pulmonary artery.

DR. CHRISTIAN: Yes, if you represent the pulmonary artery by my two fingers (demonstration with hand) the left auricular appendage just shows to the left and below it. What do you call that part of the heart just below the pulmonary artery—just below the pulmonary valves? Do you remember the name of that?

STUDENT: I do not remember it.

DR. CHRISTIAN: It is called the conus arteriosus. It comes up in a sort of cone shape, emptying into the pulmonary artery. The pulsation up here is largely due to the pulmonary artery and that part of the right ventricle that opens into the pulmonary artery, the conus; whereas if the auricle comes forward in that region it very rarely pulsates visibly or it is very rarely large enough to give any pulsation to the chest wall that you can feel. There is enough difference in the time relations of contraction of those parts of the heart to give that difference between the retraction in that place and the elevation there. The wave runs up, so to speak, over the heart.

DR. CHRISTIAN: Where does the right auricle come in the outline of the precordium?

STUDENT: The tip is over in here.

DR. CHRISTIAN: Where is most of the right auricle?

STUDENT: It is on the right side behind.

DR. CHRISTIAN: No, most of the right auricle is at the right and extends well back. Practically all of the right border of the heart except a small area is made up of right auricle. Most of the effect of changes in the right auricle as you examine the chest is shown in changes in the right cardiac border. If the right auricle enlarges, the right border goes to the right. If that dilates moderately you do not see any pulsation because the bulk of the right auricle is under the sternum. If markedly enlarged, pulsation is not visible usually, because auricular pulsation is weak.

DR. CHRISTIAN: We have here a slow regular pulse-rate and you can see a jugular pulse that is going apparently faster than the arterial pulse; what would you say was a possible mechanism working in the heart to produce those results?

STUDENT: Partial block.

DR. CHRISTIAN: What do you mean by partial block?

STUDENT: The auricle is beating faster than the ventricle and all impulses from the sino-auricular node are not causing ventricular contractions.

DR. CHRISTIAN: What sort of a relation do you have to have between the auricle and the ventricle under those circumstances to give you a regular pulse?

STUDENT: Every contraction from the auricle would be transmitted down to the ventricle

DR. CHRISTIAN: That is the normal relation. I mean what sort of a partial block would you have that would give you a regular ventricular pulse?

STUDENT: Every second beat of the auricle would not be transmitted.

DR. CHRISTIAN: Yes, you would have to have a block in which every second beat or second and third beat, etc., of the auricle was not responded to by the ventricle and then you would have a regular rate. Ordinarily with partial block we may have that, or we may have two beats and then the third one dropped out, giving a regular irregularity, or you might have three or four beats and then one be dropped out, which would still give a regular irregularity, but if you have an occasional beat dropped out you would get an irregular type of irregularity.

DR. CHRISTIAN: Why is the pulse as slow as that in partial block?

STUDENT: The ventricles contract just about half or less than the normal.

DR. CHRISTIAN: Yes, the normal rate you see is about 80, and if every other beat is dropped out you have a pulse at about that rate—35 to 40. Suppose you had a still slower pulse, would you still think it was a partial block?

STUDENT: It might be, or it might be complete.

DR. CHRISTIAN: Yes; the slower the rate, the greater the probability of the block being complete. Partial blocks are much more apt to give more rapid rates than 40. One reason is that most of those cases have a certain amount of cardiac decompensa-

tion, and the heart, if it were not for the block, would be going faster than the normal, so that though many beats dropped out, the reduction in the rate would not be great. You cannot tell from such observation as we have made whether there is partial block with just every other beat dropped out or one with two or three auricular contractions and then a normal ventricular contraction, or whether it is a complete block. All you can say is that we have a patient with arteriosclerosis, with an enlarged heart, having a very slow regular rate, but apparently in the neck you can see more pulsations than should go to the number of ventricular pulsations that you can see over the heart or at the radial or brachial artery, and that all suggests heart-block. If you take a pulse tracing with a tracing of the vein you get graphic evidence, or if you take an electrocardiogram you get graphic evidence of what is going on. There are the electrocardiograms (Fig. 82) taken from this patient. What is the first thing that strikes your eye in looking at any one of the leads as a departure from the normal?

STUDENT: The "R" wave is down in Leads 2 and 3.

DR. CHRISTIAN: That is the ventricular complex. The "R" wave is down in Leads 2 and 3 and up in Lead 1. That marked difference indicates a muscle preponderance on one side or the other, that is hypertrophy; and in this particular form in the first lead the ventricular complex mainly up and in the third down, left-sided hypertrophy which fits in with what we talked about—enlargement of the heart, a forcible apex-beat, etc. As far as the ventricular complex is concerned there is left-sided hypertrophy. Then they are quite far apart, indicating a slow rate, and they come regularly. What comes in between those up-and-down strokes? Taking that lead (Lead 1), what sort of waves appear in between?

STUDENT: Two waves.

DR. CHRISTIAN: There are two waves very much alike in that particular place. The thing to do when you are analyzing any one of these curves is when you find any particular kind of wave that catches your eye to run your eye along the record to see when it recurs, if it is just the same in form, and how many there

are, and what relation they have to some other kind of a wave that you pick out in the same way, following along with your eye. In

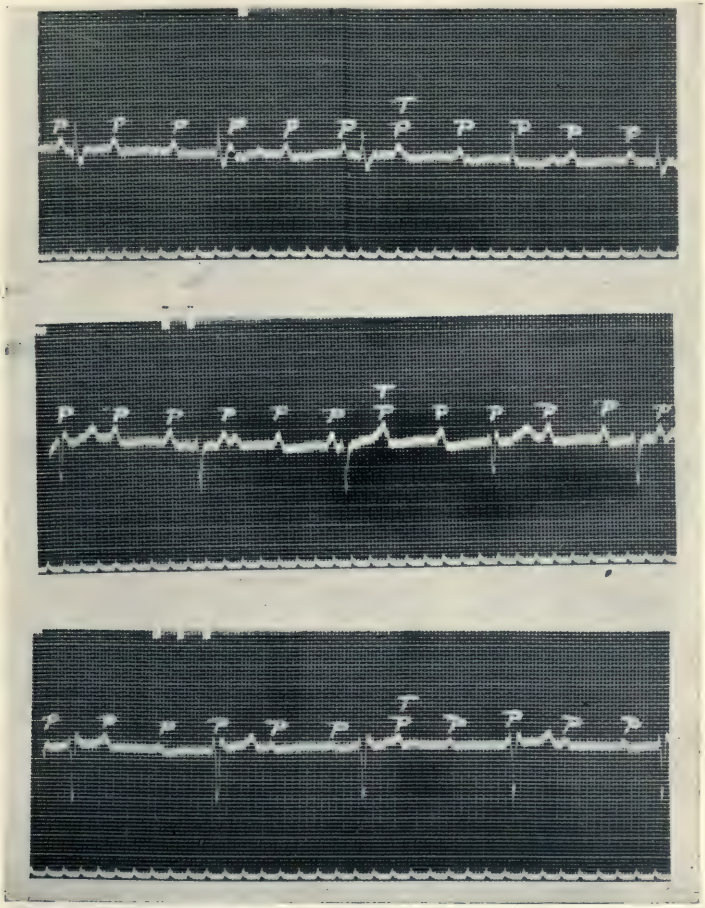

Fig. 82.—Electrocardiogram of patient No. 7345. *Diagnosis:* Complete heart-block; left ventricular hypertrophy. Auricular rate 132 per minute; ventricular rate 37. *P* indicates contractions of the auricle and the larger unmarked waves indicate ventricular contractions. Note that both auricles and ventricles are contracting regularly, but the contractions of the auricles bear no fixed relation to those of the ventricles.

analyzing these curves look to see whether a particular kind of wave that you pick out occurs regularly and evenly spaced. You can measure the distance between the beginning of different

waves and when the waves come at regular intervals you conclude they are the same things if they have the same form, and that each wave is caused in the same way and represents a definite part of the cardiac cycle repeated at a regular rate. Studying the curves this way you find a regular sequence of two types of waves ("P" waves and "R" waves), but with no constant relation to each other.

That is a case not of partial block, but of complete dissociation. The auricles are beating regularly at one rate and the ventricles are beating regularly at a different rate. One is approximately twice as fast as the other, but there is no constant relation between "P" and "R" waves. Dr. Drinker in making the curves has counted out the auricles going at a rate of 132 per minute, and the ventricles going at a rate of 37 when he took the tracing. It is a case of complete heart-block in a patient with a very considerable degree of arteriosclerosis and a hypertrophied heart without any valve lesion at all. The heart sounds are normal. There is a little soft systolic murmur that is very common in cases of heart hypertrophy when there is no real valve lesion. Heart-block occurs in people that have simple arteriosclerosis; it occurs in syphilitic cases. The Wassermann reaction has not been done on him yet; that will be reported on later.

We have not a very satisfactory history of the patient because he is an Italian with a rather limited knowledge of English. The patient says that previous to a year ago he had no symptoms at all from his heart or lungs. A year ago he fell two stories while working and broke his left ankle. Also he injured his arms and his hip. He injured himself pretty seriously, because he was taken to the Boston City Hospital and remained there two months with his leg in a plaster cast. Probably he fractured his leg. The patient states that in the City Hospital he began to notice dizziness and blurring of vision. This came on periodically. He does not think that when at the City Hospital he had anything the matter with him except as the result of the fall. At the end of two months he left the hospital against advice. He stayed about the house at home for about a month. While at the hospital before he went home he had noticed dizziness and he

at several times had fallen over, although he never hurt himself in any of these falls. He says for the past eight months these attacks of dizziness came on once or twice every day. Quite often he had had to lean up against a building or catch hold of something to keep him from falling down. He had never vomited in any of these attacks. Several times while out on the street he has been mistaken for being drunk, and on one occasion he was actually arrested. (It is not very long since we had another patient with pathologic dizziness who was arrested for drunkenness. That shows the activity of our police and sometimes their failure to discriminate.) He has been unable to do any work and scarcely ever goes out of the house for any length of time without having these attacks of dizziness come on. Naturally, he is afraid to go out. During these attacks his eyes begin to roll, things go round in circles, and very often during these attacks he has palpitation of the heart. There is no history of any loss of consciousness. There have been no attacks of nocturnal dyspnea, no cough, no swelling of the feet or abdomen. He says that if he talks for any length of time he gets very dizzy and very short of breath.

His history as far as we know, but we are not absolutely certain, dates back for about a year and consists in recurring attacks of dizziness and enough of that to keep him from work and pretty well confined to the house, and yet he has never had any severe dyspnea or any edema indicating a decompensated heart, nor has he had any attacks of actual loss of consciousness.

It is a little difficult to explain just why he should have dizziness in recurring attacks. It may be that his heart-rate varies from time to time, and if it slows beyond a certain point, nutritional disturbances in the brain result from the slowed circulation and bring on the dizziness. Since we have observed him in the hospital on only a few days have there been any very marked variations in his pulse-rate. Some of these cases of heart-block have periods in which the heart slows down very much in rate; it drops down to 10, 12, 14, or something like that. Those patients then become dizzy or lose consciousness. He may have had something of the same nature, but not a drop in rate slow

enough or of long enough duration to produce unconsciousness. When they lose consciousness we speak of that as Stokes-Adams disease or Stokes-Adams syndrome, named for two Irish physicians who a good many years ago described these cases of abnormal slowing of the pulse accompanied by attacks of unconsciousness. It is not proper to call the condition Stokes-Adams disease unless there are definite attacks of loss of consciousness. Recurring attacks of dizziness in a patient with a slow pulse are not to be called Stokes-Adams syndrome. Consequently we simply speak of this as a case of complete heart-block—complete dissociation between the auricles and the ventricles, and not a case of Stokes-Adams disease.

We see dizziness also in a number of our patients who have a normal heart-rate, but who have a high blood-pressure or have arteriosclerosis, or both, so that the attacks of dizziness in this man may be associated only in part with the slow heart-rate, and in part we can associate the dizziness with the high blood-pressure and the arteriosclerosis which he has. Arteriosclerosis causes attacks of dizziness not because the peripheral vessels are sclerosed, but because the cerebral vessels are sclerosed. We take it for granted that if the peripheral vessels are sclerosed there is probably sclerosis of the cerebral vessels. As this man has marked peripheral sclerosis we think very likely his cerebral vessels are sclerosed also. That and the high blood-pressure may produce his disturbance. The cases with sclerosis and high blood-pressure often do have temporary attacks of dizziness. The sclerosis does not change, that is a slowly progressing process. It cannot change from hour to hour or day to day. The blood-pressure, as a rule, as far as we have observed it does not vary suddenly in these cases, so we have to assume that the dizziness is due to some other circulatory disturbance than change in blood-pressure or change in heart-rate or change in the vessel wall, and various theories have been advanced as to just what takes place. Most of them ascribe the cause to some form of transitory anemia or transitory edema of the brain in some way related to the poor circulation in a case with thickened vessels and hypertension. As I have said, we see a great many cases of high tension and

sclerosis with dizziness. Complete heart-block is a much more unusual condition, and those cases sometimes have these attacks of dizziness, but just whether the attacks of dizziness are due to slow rate, hypertension, or arteriosclerosis we cannot say. Very likely all three play a part. This patient also has a considerable amount of abdominal discomfort. He seems to complain a good deal of his abdomen. Possibly he also has arteriosclerosis in his abdominal vessels and has disturbance from that.

October 15, 1917: The patient that I showed you at the last clinic, the Italian with the heart-block (P. B. B. H., Med. No. 7345), has made no change since you saw him. He is still in heart-block, but we have this added feature in his case that we did not have at that time, we know that he has a double positive Wassermann reaction, so that antiluetic treatment will be instituted and we will watch the effect as indicating whether or not he has some luetic lesion causing the block, and in that case one that will clear up under antiluetic treatment. When I showed the patient, his blood had just been sent down to the laboratory for the Wassermann reaction. It was done the following day and was confirmed by repetition, both times being double plus.

November 6, 1917: You may be interested to hear of the patient that I showed at an earlier clinic, the case (P. B. B. H., Med. No. 7345) of complete heart-block. That patient with the complete heart-block and positive Wassermann reaction is still in the ward. He is having antisyphilitic treatment and it is not doing him any good, that is, the heart-block continues, and his signs of heart-block and his symptoms are probably more marked than when I showed him to you. The night before last his pulse went down to 18 and during that time he complained, as he did before, of abdominal pain and of dizziness, and with this slowing of the pulse he got an attack which I think probably is best explained as hysteric manifestations. He writhed around in bed, groaned, mumbled, etc., and I think part of that is hysteria probably due to the fear of impending death or something of that sort with slowing of the heart-rate. Notwithstanding the positive

Wassermann reaction the treatment has not produced any change and the block has continued, and with the complete block at times his idioventricular rate slows down. The slowest that has been counted so far is 18 per minute. He has no signs of cardiac decompensation.

PARTIAL HEART-BLOCK WITH STOKES-ADAMS SYNDROME. DIGITALIS HEART-BLOCK IN AURICULAR FIBRILLATION

PARTIAL HEART-BLOCK

October 16, 1917.

DR. CHRISTIAN (to a student): Please take this man's pulse (P. B. B. H., Med. No. 7374) and see what you make out.

STUDENT: It is an irregular pulse, rapid and weak, and the beats vary in character.

DR. CHRISTIAN: How fast is it?

STUDENT: 108.

DR. CHRISTIAN: It has been running in the ward, as a rule, more slowly than that. Most of the counts have been about 80. They run from 95 as a high level down to 60 as a low level. Just now I should think it is not very much faster than about 85 as I feel it. What is the type of irregularity? What did you notice?

STUDENT: It is irregular in time and there seems to be a skipped beat.

DR. CHRISTIAN: What do you mean by that—skipping like someone skipping rope?

STUDENT: It goes rapidly for eight to ten beats and then it slows. I think it goes slowly for three or four beats and then returns to the rate it was going at before. There is not any great change between those periods.

DR. CHRISTIAN: There are three or four beats at a certain speed and then three or four at a slower rate and then restoration of the previous rate. We do not call that skipping beats. What sort of an irregularity is that—periodic slowing and increasing in speed, three or four slower and then three or four faster, and then three or four slower again—what would you say that was?

STUDENT: A sinus arhythmia.

DR. CHRISTIAN: Yes, that is a sinus arhythmia. Keep feeling the pulse and tell us if you get any other form of irregularity. What did you get then?

STUDENT: A dropped beat.

DR. CHRISTIAN: What do you mean by that? Describe to the class what you felt.

STUDENT: There is a total pause between the two. The time period between those two beats is greater than the time period between two others.

DR. CHRISTIAN: Here is a heart going at a certain rate, then there is a pause, and then the heart goes on at the same rate. Did you form any idea as to how much longer a long pause was than the preceding one? That happens very occasionally.

STUDENT: Roughly, it seems to be about double.

DR. CHRISTIAN: Yes, that is about the right expression. As you feel the pulse occasionally there is a period between the beats of practically double length and then the normal rate immediately returns. The pulse is going at a normal rhythm and normal rate, and then every once in a while a beat drops out completely and nothing takes its place, but there is no other disturbance in the rhythm. This dropping out does not happen very often.

DR. CHRISTIAN (to student): Just examine the heart quickly as to size, murmurs, etc.

DR. CHRISTIAN: I will give you the patient's history while Mr. ——— is going over the heart for other abnormalities. He is forty-seven years of age and is a painter by occupation. He was admitted to the hospital on the 10th of October. His family history is entirely negative. He has been married fifteen years. His wife is living and well. There have been no children, no pregnancies, and no miscarriages. He formerly drank one or two whiskies daily for several years back, but for the past three or four months he has not used any alcohol. He chews and smokes, using 70 cents' worth of tobacco in a week. He drinks no tea or coffee. Recently he has been taking some sort of medicine given him by his doctor, but he does not know what it is. He has been a painter for thirty years. He has always taken good care to clean his hands well and has had no symptoms of lead-poisoning. He

works seven to eight hours daily and most of his work is indoors. He had to stop work on September 25th on account of the present illness. He has always lived in Boston. He had what he was told was typhoid pneumonia at the age of fourteen years. He was not seriously ill and made a good recovery without complications. He does not remember any of the children's diseases, but says that during the past eight or ten years he has had several slight sore throats lasting about a day or two, but none of these were very severe. He was asked specifically about the various common infectious diseases, but he apparently has had none of them. There is nothing in his past history of importance in regard to his head or throat. As to his cardiorespiratory history, five or six years ago he had rather sharp pains over his heart which lasted several weeks. These pains disappeared without treatment. They were sharp and stabbing, coming suddenly and disappearing suddenly. He has also noticed for two or three years that in going up steps or walking very fast or if he makes any severe exertion he becomes somewhat dyspneic and has palpitation. There is no other history of pain in the chest and no dyspnea beyond what I have given. There has been no cough or hemoptysis. He thinks that occasionally he has had night-sweats. His gastrointestinal history is entirely negative in the past. His stool has been dark for the past two weeks, but he thinks that this is due to medicine that the doctor has given him. Forty years ago he had a Neisser infection which lasted for three weeks. He was treated and recovered without complications. There has been no other urinary or genital disturbance. His present illness is as follows: On the 22d of September, while standing on the street talking to a man, the patient says he had a sudden "flash." During this time everything became dark before his eyes and things disappeared. This attack only lasted, just as he expresses it, as a flash of darkness and then cleared up. The whole thing lasted probably about two seconds, that being his idea of the time. He thought nothing about it, but next morning while walking along he had another "flash." "Flash" means apparently this temporary darkness. Along with this dark sensation he had what he called a "gone feeling" around his heart. He came very

near falling, but the whole thing was over in a short time and he did not fall. Two days later he stooped over to take up an object and on standing up again he fell over backward. He says things looked black and then he lost consciousness and fell to the floor. He states that he struck his head on a bench when he fell and that he remained on the floor for about one-half hour, but was not unconscious during all this time. (I think the period of unconsciousness was a short one and he was either afraid to get up or felt badly enough not to attempt it, or possibly he was totally unable to get up.) After about one-half hour someone helped him up and in a short time he felt all right again. During these attacks all the blood in his body seems to rush to his head, he is numb all over, and has a gone feeling over his heart. He says that some of these attacks last from five to ten seconds and following the attacks he feels bilious for awhile. These attacks have gradually increased in frequency until now after exercise or walking fast he has three or four attacks in five to ten minutes. He has never lost consciousness except in the one instance mentioned above. That is all of recent development, beginning September 22d. What do you make out about the heart; first, as regards size?

STUDENT: I do not get the left border on percussion, but the heart is very much enlarged.

DR. CHRISTIAN: The heart is enlarged, but it is not enlarged quite as much as you would make it to be. I have my finger on the apex. It is a few centimeters outside the nipple line. The exact distance for our present purpose does not make any great difference. Here is a man with a heart that is enlarged so that the apex is well outside the left nipple line. What did you hear on listening?

STUDENT: The sounds are muffled and distant. I heard a systolic murmur and a murmur which follows the second sound.

DR. CHRISTIAN: In the first place, the sounds are not very loud. In the second place, the first and second sounds are rather definitely similar in character. In the third place, there is a distinct blowing, not very loud systolic murmur heard at the apex. The same systolic murmur is heard at the base. It is probably

a little louder in the aortic area than in the pulmonic area. In the pulmonic area the second sound is immediately followed by a very short diastolic murmur. The same diastolic murmur is heard faintly at about the nipple, slightly inside the apex. There are no palpable thrills. As far as the heart goes, it is simply a heart showing enlargement with a slight blowing systolic murmur which I think only indicates a relative mitral insufficiency. The diastolic murmur is possibly associated with slight regurgitation at the aortic or pulmonic area or possibly suggests a slight mitral stenosis. The intensity of the murmur and the general character would make you think the patient essentially has no valvular lesion in the heart except simply a slight relative insufficiency of the mitral ring; in other words, it is an enlarged heart and is essentially a condition of slight chronic myocarditis.

QUESTION BY A STUDENT: Does the fact that the sounds are somewhat similar in character have any significance?

DR. CHRISTIAN: Yes, that means a disturbance in the heart muscle, the sounds approaching each other in quality. Ordinarily there is a distinct difference between the first and second sounds whether you listen at the apex or at the base. Sounds approaching each other in quality may change in two directions; either the first sound, which is normally a muffled one, can become sharp like the normal second sound, or the second sound, which is ordinarily a sharp one, may become a muffled sound and similar to the first sound. In this particular case both sounds are muffled and are similar to the ordinary type of first sound when you listen at the apex and that goes usually with myocardial weakness. The other change—the change in the other direction —suggests mitral stenosis. Did you make out anything abnormal in the neck?

STUDENT: There is a marked pulsation on the right side.

DR. CHRISTIAN: There is a very definite venous pulsation in the neck. I would not call it very marked. It is very easily seen, but you have not seen any really marked one where the veins stand out, and you can see with great intensity all the little pulsations. This is not anything more than a great many normal people have. You can see perfectly well the venous pulsation in

the neck. There is no trouble about seeing it, but what I am criticizing is that you ought not to call that marked. It is not marked. You apparently have not seen a case of marked pulsation. I will show you some before we go very far and you can see the difference. Sometimes the veins stand out like cords in the neck and you see a pulsation running up and down with every cardiac impulse, so that at the first glance at the patient you notice the striking pulsation. This is an easily visible pulsation, but it is not a very marked pulsation.

I may say that while listening to the heart I happened to catch one of those irregularities such as happened before when I was feeling the pulse, and during that interval nothing was heard at all. I mean there was no beat, no first sound, no second sound, no murmur. There was no interruption in the character of the beats or the character of the murmurs just before or after that beat was missed.

STUDENT: I find nothing abnormal in the neck unless it is that sometimes the beat seems to be followed by two sorts of waves.

DR. CHRISTIAN: Yes, sometimes you see a double wave; a more prominent one and then a less prominent one. Is that abnormal or normal?

STUDENT: I should think that was normal.

DR. CHRISTIAN: Yes, that is normal. As I have said before, there are three waves ordinarily in the venous pulse as traced by graphic methods, but you do not, as a rule, see more than two. To see two waves, one a little larger and one smaller, is a normal thing, and you are perfectly right in saying that is a normal looking venous pulse in this patient. If you happened to look when those beats dropped out you would see something different. That happens only occasionally, and ordinarily as you watch that it is a perfectly normal jugular pulse in the neck. It is quite easily seen, but that does not constitute any great abnormality. That is essentially all that is to be made out on physical examination of the patient. Everything else is normal.

Now we will take up the analysis of that irregularity and see what we find. Here is a tracing (Fig. 83) taken when the patient

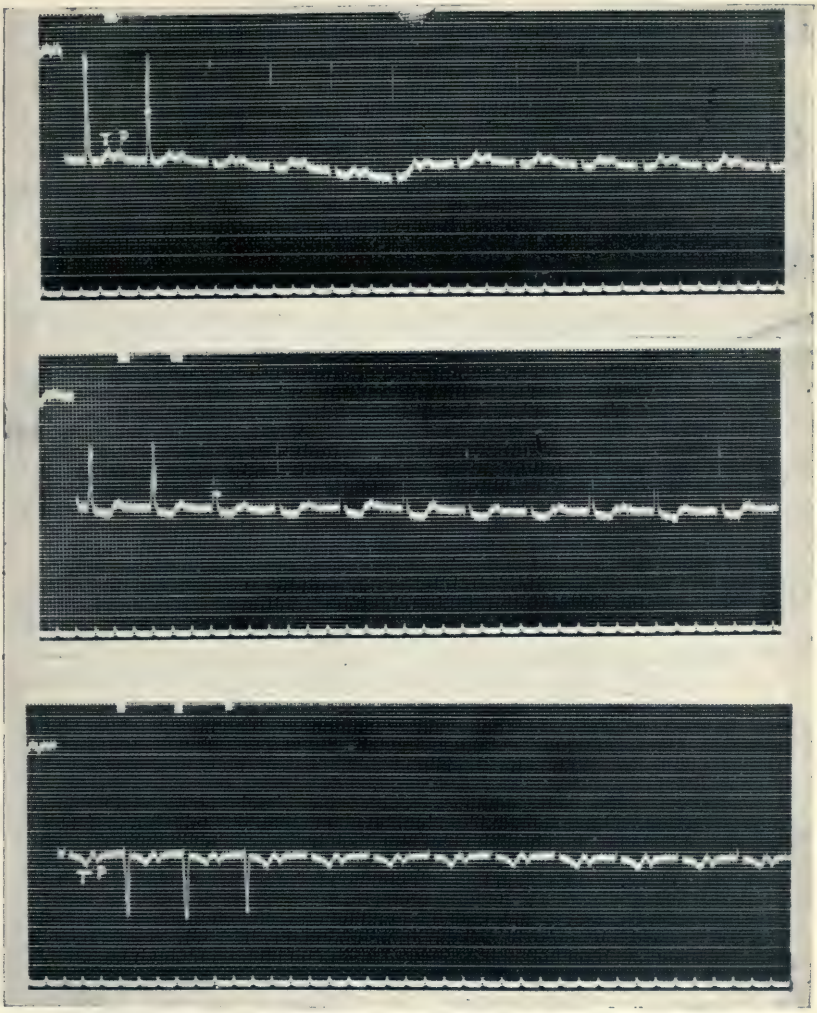

Fig. 83.—Electrocardiogram of patient No. 7374. *Diagnosis:* Delayed conduction time, *P–R* intervals 0.36 second; left ventricular hypertrophy. *T* indicates wave marking the end of the ventricular activity. *P* indicates wave corresponding to the contraction of the auricle. The larger unmarked waves represent the wave of the early activity of the ventricular contraction. Note the increased interval between the contraction of the auricle (*P*) and the beginning of the activity of the ventricle.

was quietly lying in bed. See if you find any irregularity in that? These very fine lines represent the ventricular contractions. It

happens that the electrocardiogram was taken with a very fine string and the line of the ordinary wave of the ventricular complex is not very marked. The string moves up and down very quickly, making a very fine line. As far as that goes, the ventricle is beating perfectly regularly in this lead. That is the "T" wave completing the ventricular complex and those are the "P" waves. What would you say about the "P" waves in relation to the ventricular complex?

STUDENT: They are more removed than normal from the ventricular beat.

DR. CHRISTIAN: Yes, they are more removed. The time between "P" waves and "R" waves, in other words, conduction time, is eight-twenty-fifths to nine-twenty-fifths of a second. The normal conduction time is one-fifth of a second or a little less. We are dealing with a patient whose heart is regular, but who has delayed conduction time, and that delay is practically twice the normal. It takes twice as long for the impulse to go from the auricle to the ventricle in this particular patient as is normal, and over long periods of time that happens, and nothing else. You remember he says that following exercise he has what he described as these "flashes," coming on suddenly, then disappearing, and he has the feeling as if his heart stopped in that period, so we gave him a little moderate exercise, having him stand up and lie down, and in an electrocardiogram taken immediately after that exercise you notice in the first place a regular rate over most of it with delayed conduction time, and at one point the period between the ventricular complexes becomes practically twice as long as the regular rate. When that happens there are two "P" waves and between those two "P" waves there is no ventricular complex; in other words, strictly speaking a dropped beat or a blocked beat brought on by exercise—delayed conduction without exercise, with exercise some blocked beats. We have repeated that on other occasions. On the 13th of October before exercise there was occasionally a dropped beat, and after exercise rather more frequently these dropped beats.

QUESTION BY STUDENT: How can you tell that that is a "P" wave and not a "T" wave?

DR. CHRISTIAN: From its relation to the "R" wave, the relation in different leads always being the same. When Mr. ——— passes those others around you will see that the "T" waves are all inverted in the next curve and unlike the "P" waves. If you look closely in the other lead you will see that the "P" wave is not exactly like the "T" wave. The "P" waves are the same as repeated and the "T" waves are the same, but they are different from each other.

That is the other picture of heart-block. I showed you before (P. B. B. H., Med. 7345) the patient with heart-block where there is complete dissociation; the auricles and the ventricles beating independently in a patient with marked arteriosclerosis and a large heart, and, as subsequently added, a double positive Wassermann reaction, and his symptom was frequent dizziness, no loss of consciousness. Here is a patient who has once lost consciousness and immediately following exercise has a delayed conduction changed into a partial heart-block and has sensations at that time depending upon how many beats drop out or how slow his heart-rate becomes. Probably the time he lost consciousness his rate slowed down to one-half of the normal or possibly less. Recently his heart has been going at about a normal rate with an occasional dropped beat. That, so far as he has had attacks of loss of consciousness, etc., is a case of Stokes-Adams disease. It is not a well-marked case such as we may possibly see later on. That condition was recognized in the ward before electrocardiograms were taken on the basis of the man's description of his attacks and feeling these occasional beats that simply disappeared—dropped out. We were not at all surprised when we got an electrocardiogram to find the man had a disturbance in conduction time. In fact, notes were made in the history before any electrocardiograms were taken that it was probably a case of heart-block with Stokes-Adams disease. I am emphasizing that simply to bring out the point that it is possible in these arhythmias to form a pretty good idea of what is going on in many of the cases, and by that I mean the mechanism of the irregularity, without having elaborate means, either polygraphic or electrocardiographic, of recording the irregularity. The

Wassermann reaction is negative in this patient. Syphilis is not an etiologic factor. There is not a very marked change in the blood-vessels. Possibly there is a little arteriosclerosis. He is a painter, but so far as we know lead has never produced any serious damage in him. He has never had lead-colic, never had a dropped wrist, or any of the other symptoms of lead-poisoning. His heart is enlarged and the sounds indicate a myocarditis. As far as we can go he is a patient with a myocardial disturbance. In various places in the heart there is some sort of lesion, and among other places there is a lesion that interferes with his conduction time and slows it to one double the normal length, and very often, particularly after exercise, the ventricular beats drop out altogether.

QUESTION BY A STUDENT: Are you more apt to have Stokes-Adams syndrome with partial block than with complete?

DR. CHRISTIAN: It does not follow any definite rule. The syndrome comes when the heart occasionally slows down enough to give poor circulation to the brain. If you get anemia you get loss of consciousness or irritation, and if irritation, you get convulsive seizures, and that is all you can say. That might come in complete block or it might come in partial block. Probably more often it occurs with complete dissociation than with partial block. Stokes-Adams syndrome is much more infrequent than heart-block, *i. e.*, we see many cases of heart-block of various types which do not have the Stokes-Adams syndrome.

November 6, 1917.

DR. CHRISTIAN: The patient (P. B. B. H., Med. No. 7374), who had pretty definite Stokes-Adams syndrome of a mild character with delayed conduction time and increased block brought on by exercise, we put on thyroid extract following a suggestion which came from Dr. Blackford of the Mayo Clinic,[1] that as thyroid had an influence in increasing the heart rate, it might have an effect on the patient's block. As a result of thyroid medication in our patient the auricular and ventricular rate increased and conduction time decreased. He left the hospital

[1] Blackford, J. M., and Willius, F. A., Amer. Jour, Med. Sci., 1917, cliv, 585.

some ten days ago, and before he left we were no longer able to produce any of those periods of heart-block. You remember we brought on definite block when he first came in by having him exercise a little bit. Just before he left we ran him up and down stairs trying to produce a block, but could get none (Fig. 84, electrocardiogram of October 23d after exercise). He could go up and down stairs perfectly well, and do such things that he had been unable to do since these attacks developed. He went out to continue taking the thyroid until he got some signs of thyroid intoxication. What will be the permanent result on that patient I have no idea, but as far as seen from our observation thyroid increased his heart-rate, and in doing that had not simply an effect on the auricle and ventricle, but there was an increased rate of conduction, so that the slowed conduction time, whereas it had not come to normal when he left, had been reduced to almost a normal conduction. As I remember it, it was almost two-fifths of a second when he came in and it was somewhat over one-fifth of a second when he left. The symptoms of block disappeared with that change in his conduction time after using thyroid extract.

Subsequent Note.—After leaving the hospital the patient took thyroid extract for one week, then discontinued it. After a few days his symptoms returned and increased in severity. He came back to the hospital and was found to have complete heart-block. Thyroid extract was begun again. The first few days in the hospital the patient was very uncomfortable, had periods of unconsciousness, and a slowed heart-rate. At times there would be intervals as long as fifteen seconds between ventricular beats. Gradually the block decreased, and on December 8th electrocardiograms showed no blocked beats, his pulse was regular, but the conduction time was delayed as it was on his first admission.

DIGITALIS HEART-BLOCK IN AURICULAR FIBRILLATION

DR. CHRISTIAN (to a student): I wish you would come down and feel this patient's pulse (P. B. B. H., Med. No. 7313).

This patient is thirty-six years of age. Her family history is negative. She was born in Russia and has lived in Boston for

fifteen years. She had measles as a child. She has had tonsillitis five or six times; the first time fourteen years ago, the last time one

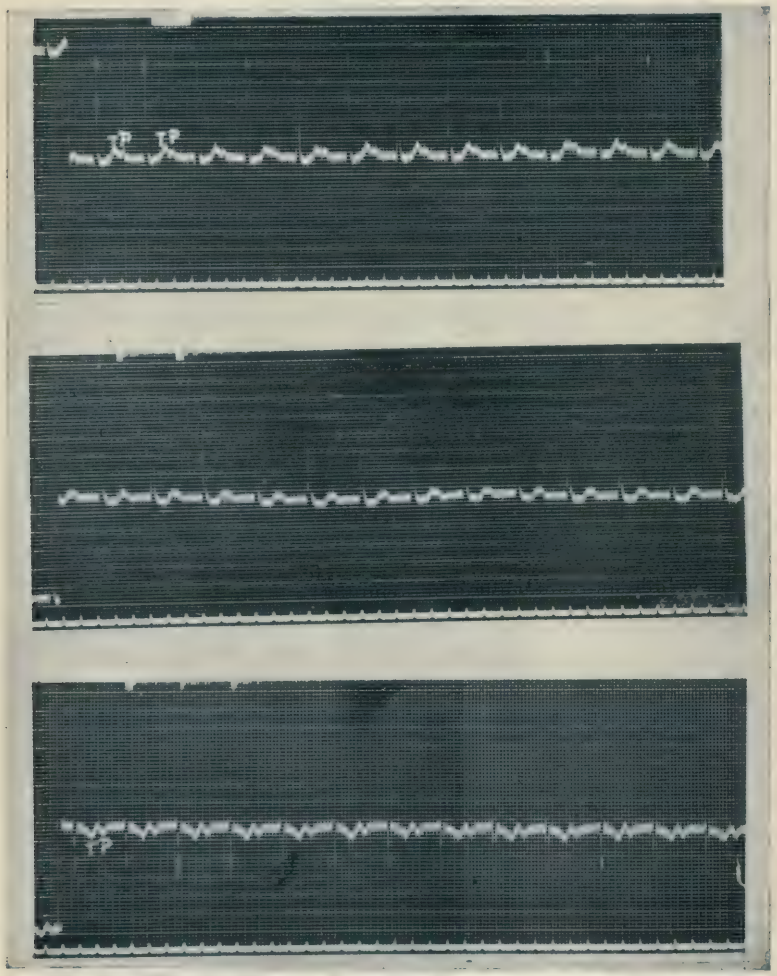

Fig. 84.—Electrocardiogram of patient No. 7374 taken five days after the electrocardiogram shown in Fig. 83. *P–R* interval has shortened and is now 0.28 second following thyroid extract, 0.13 gram three times a day.

week ago. She had an attack of rheumatic fever six years ago. She was ill in bed at that time for three weeks. There is no history of any of the other acute infectious diseases. For the last six

months the patient has noticed black spots before her eyes, but no failing vision, no inflammation of the eyes, and no pain in the eyes. She has had frequent attacks of tonsillitis which I have already referred to. Her gastro-intestinal history is entirely negative. Her genito-urinary history is entirely negative. She has lost weight. A year ago she thinks she weighed 170 pounds. Now she weighs 135 pounds. Her present illness seems to date back quite a period—to ten years ago following a very severe attack of tonsillitis. On recovering from this she fainted on several occasions. A local physician who was called in told her that she had heart trouble. That was ten years ago, and at that time she was very edematous and had sharp, stabbing pains over the precordium. She was kept in bed for eight months. She then got up and felt well until two years ago, when she fainted while washing clothes. At this time she had no palpitation, but did have slight edema. Followng this attack she did her own work about the house, getting along fairly well until three months ago. At that time she began to cough and about this time she became short of breath. Palpitation became very troublesome and her legs became very much swollen when she was up and about on them. During the past four weeks she has been in bed most of the time. Five days ago she became very dyspneic. On several occasions she has had a sharp pain in the epigastrium, radiating through to the back. These pains come on suddenly at any time and usually last about one hour.

What do you make out in her pulse?

STUDENT: She has a very irregular pulse. There seemed to be three or four strong beats, then a long pause, then sometimes one more strong beat and then a pause. Sometimes there are longer pauses, at other times I feel every beat fairly strong for eight or nine beats. The pulse is 48.

DR. CHRISTIAN: I do not know whether you thought a good many of the beats were strong beats, or did you say you felt some weak beats or not?

STUDENT: I did feel weak beats every now and then.

DR. CHRISTIAN: How did those weak beats come in relation to the strong ones?

STUDENT: To me they seemed to come after the pause. There would be a strong beat, then a pause, then a strong beat, and then the next two or three beats would be weak.

DR. CHRISTIAN: Did you feel any other weak beats?

STUDENT: Just then I felt a rather accelerated beat.

DR. CHRISTIAN: The heart is beating along with pulse-waves of about the same character, and then very shortly after one of those normal pulse-waves you can every now and then feel a very faint pulsation. It is just detectable to the palpating finger. Then it may go along for quite awhile, as you described it, quite regularly, all the beats of the same size and about evenly spaced. It has been some time now since I felt one of those little beats. As I feel it now it is beating quite regularly and beating at a distinctly slow rate. I felt then just a little beat. You felt a succession of small beats. Since I have been following it I have not felt that. I do not doubt that at times that is present, but it happens only very occasionally. At times you get a much weaker beat, and then a little bit more of a pause, and that is repeated several times, and then you get periods in which you get just a succession of rather normal beats, apparently quite regular and at a slow rate. Then there are periods when, as you described it, I did not feel it, there is quite definite irregularity and a succession of quicker beats, irregularly spaced, some smaller and some larger, but, in general, weaker than those recorded before. That is probably what is going on. It is a heart that varies quite a good deal in its succession. Sometimes such an irregular beat as that coming on shortly after a normally spaced beat is an ectopic beat; it is an extrasystole originating from some point or other in the heart. Its strength varies with time relations. If it comes quickly after a strong beat it comes at a point when two things are happening in the heart. First the heart is filling up and necessarily contains very little blood, and consequently if it comes when contraction has taken place recently it can make only a small pulse-wave because the systolic output is very small. Or if it comes close to the regular beat it strikes in the fag end of the refractory phase, and whereas the heart

muscle responds to the stimulation, it does not respond with a very forcible contraction. Those two things together give a small pulse-wave.

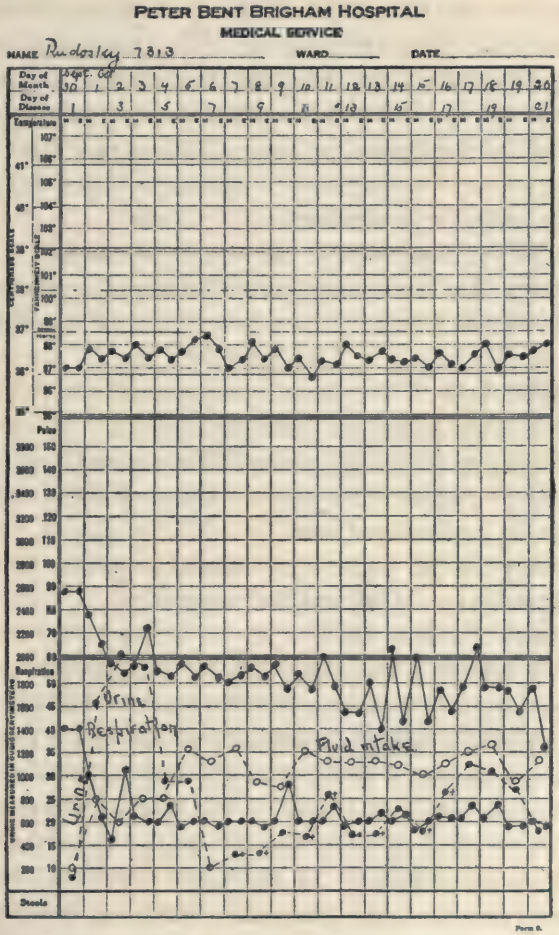

Fig. 85.—Chart of patient No. 7313. *Diagnosis:* Auricular fibrillation with heart-block produced by digitalis. Note the decrease in pulse-rate and the diuresis following digitalis.

DR. CHRISTIAN: (to student): Won't you listen to the heart to see if there are any murmurs?

The point of interest in this patient's chart (Fig. 85) is that when she came in her pulse was running at a rate of 90, and

then dropped on the third day to 60 or less, and it has been below 60 ever since she has been in. It has been counted down as low as 45 and 40 in the last few days, so that she has had a slow pulse since she has been in the hospital. I will read the description of her pulse when she came in: "The pulse-rate was 90 per minute, pulses equal, very irregular in force and rhythm. Vessel wall not palpable." You see there was no dominant rhythm. It was absolutely irregular and on the basis of that absolute irregularity the patient was diagnosed as having auricular fibrillation—I mean by the pulse observation.

What do you make out in the way of murmurs?

STUDENT: The first sound seems to be rather distant. The second sound has a rolling character to it as if it were reduplicated.

DR. CHRISTIAN: You have really put the cart before the horse. You have mixed up those two sounds. The first sound has the rolling or rumbling quality. The second sound is short. The rumble is with the first sound. Did you listen at the base? Were there any murmurs there?

STUDENT: In the aortic area I heard a systolic murmur.

DR. CHRISTIAN: Did you feel anything?

STUDENT: I felt a thrill.

DR. CHRISTIAN: Yes, those are the main points. I do not want to go into the discussion of valve lesions. Here is a patient with a perfectly definite abnormality of her heart sounds with a thrill and murmurs. It happens she has a systolic thrill that is pretty intense over the base of the heart accompanied by a harsh systolic murmur. She has also in the same region a prolonged diastolic murmur. In the apex region she has just a slight thrill, presystolic in time, has a rumbling first sound, and a blowing systolic murmur. She has, as far as her valves go, the signs of aortic stenosis as the most striking thing; with the stenosis is aortic regurgitation. There are signs at the apex that are suggestive, but are not exactly diagnostic, of a mitral stenosis. She also has a regurgitation through the mitral valves or mitral insufficiency. I say "suggestive" and not "diagnostic" because of the possibility of it being the Austin-Flint type of

murmur, which we find, according to the text-books, associated with aortic insufficiency; according to our own idea here we do not take much stock in Austin-Flint murmurs. When the murmur is quite definite we call it mitral stenosis, and we have pretty good reason to think that under those circumstances we are quite correct, because when we get a chance to view the heart we find stenosis present in proportion to our finding the signs of it. We very rarely make a diagnosis of an Austin-Flint murmur.

She has an enlarged heart with valve lesions. When she came in she had this absolutely irregular pulse which we regarded as due to auricular fibrillation. When she first came in we gave her a brief period of digitalis and her pulse became quite regular. There was no longer any variation in the time between succeeding beats. They were all of the same character as far as the strength of the pulse-waves were concerned. When we studied them with the electrocardiograph (Fig. 86) we found that the ventricles were beating perfectly regularly and that the auricles were not beating at all except in fibrillation. All that could be seen in that electrocardiogram would be a ventricular complex, then a string that did not do anything except have a lot of fine movements in it, little fibrillary twitchings, until the ventricular complex was repeated. That is a different kind of heart-block. This patient is at this time in complete heart-block. Complete heart-block has been produced therapeutically in all probability; that is, by giving digitalis we have decreased the irritability of the conduction system so that it no longer conducts the various types of impulses sent out from a fibrillating auricle. The auricles continued fibrillating just as they were before, the ventricles were beating at a more even rhythm, and that was a rhythm most of the time between 50 and 60, perfectly regular, and the patient was very comfortable. After a time the block did not persist and in the last day or two we have had what was described here—occasionally an extrasystole and occasionally periods in which the heart was absolutely irregular as described; that is, a succession of quicker beats, varying in intensity and vary-

ing in the space between each successive beat; in other words, a heart partially out of block. I have one electrocardiogram

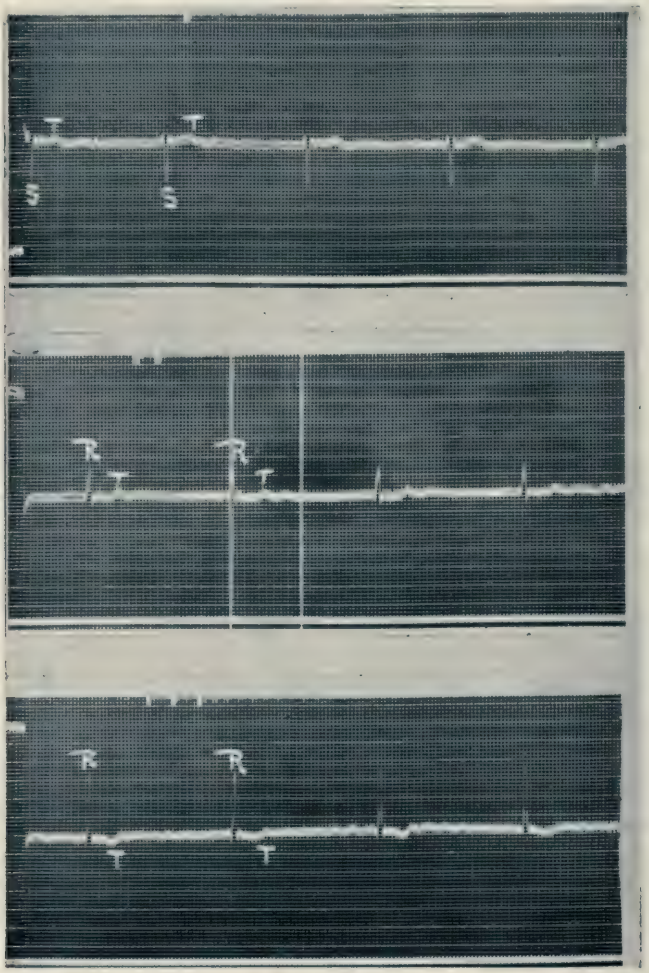

Fig. 86.—Electrocardiogram of patient No. 7313. *Diagnosis:* Right ventricular hypertrophy; auricular fibrillation; complete heart-block. *R* and *S* indicate the wave of the beginning of ventricular activity; *T* wave marks its end. Note the absence of *P* waves and the regularity in rate in the occurrence of the *R* and *S* waves.

(Fig. 87) here that just happened to catch an ectopic beat and that is in the middle one of these three tracings. You will

notice a regular slow rate except at one point when it was interfered with by the ectopic beat. That is a different kind of ventricular complex coming closely after the regular one and

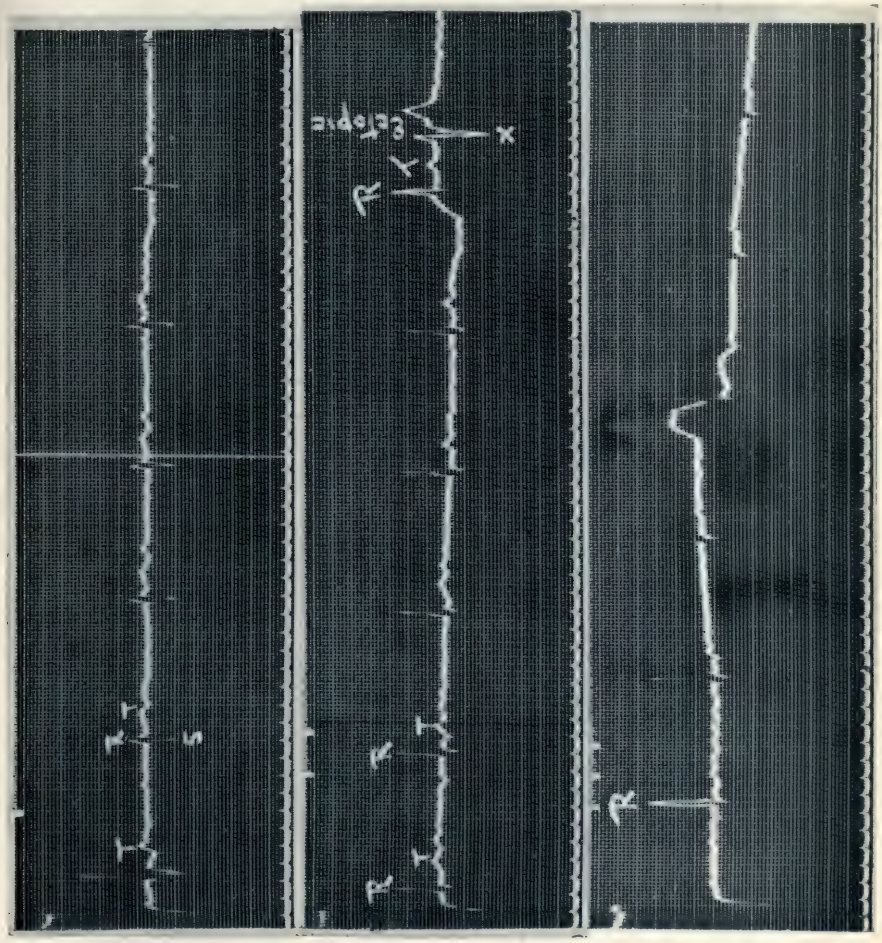

Fig. 87.—Electrocardiogram of same patient as shown in Fig. 86. Note the regularity in the recurrence of the *R* and *S* waves, the absence of *P* waves, and at *X* an ectopic contraction of ventricular origin. Note in this the difference in form from the preceding *R* and *T* complexes.

of an abnormal form and consequently an ectopic beat. We recognize that as an ectopic beat because of this abnormality

in form. You see it is in a different direction from these other regular ones. It is longer than the other regular ones and has an exaggerated "T" wave. It comes shortly after the regular "R" wave, but does not particularly disturb the rhythm. Here is a condition of transitory complete heart-block in a patient with auricular fibrillation, and it is produced, as I say, probably by digitalis. It did not exist when the patient came in. We gave the patient a short course of digitalis. Her heart went into complete block and remained regular for five or six days, and then the irregularity that she formerly had began again to make its appearance. We see that very often; we produce the block therapeutically.

I want to contrast the three cases of heart-block (Clinics of October 8th and 16th) from this point of view. The first patient (P. B. B. H., Med. No. 7345) had complete dissociation and had the symptoms of dizziness, the lesion probably was of syphilitic origin, as he certainly had syphilis. The second patient (P. B. B. H., Med. No. 7374) had a regular heart-rate most of the time with delayed conduction time, and occasionally as the result of exercise or a strain his heart went into partial block, and when it went into partial bock he had what he described as a flash of darkness, and on one occasion, presumably when it remained in block for a longer time, he lost consciousness. He became unconscious, but did not have any convulsions. In so far as loss of consciousness in this definite attack goes he has Stokes-Adams syndrome in association with heart-block. After a time he developed complete block, and later this disappeared and he returned to a regular rhythm with delayed conduction time. Both of those patients are uncomfortable in relation to the block, the kind of the block, the amount of the block, etc. The other patient (P. B. B. H., Med. No. 7313) with auricular fibrillation is comfortable when her heart is in block and uncomfortable when her heart is out of block. The third case of block was produced therapeutically, the result of producing the block is getting her heart going regularly at a rather slow rate and with a ventricular contraction with each beat a functioning beat in the sense of a good systolic output. When she

has that her circulation is better and she is more comfortable. When she passes out of block this fibrillary twitching in the auricle begins to effect the rhythm of the ventricle and changes the rhythm from a regular slow rhythm to an irregular rhythm, and as the block disappears to a faster rhythm. With that irregular rhythm some of the beats are of too little force to make much of a systolic output, many of the beats come out of time when there is not very much blood in the ventricles, and consequently the systolic output is small. That patient is uncomfortable just in ratio as the block decreases. The other patients you might say are uncomfortable just in ratio as the block goes the other way—the more block, the more uncomfortable; in the fibrillating case the more block, the more comfortable.

We see a good many cases in which varying degrees of heart-block are produced by digitalis in these fibrillating hearts. That is the way to treat the heart, and our treatment is successful in so far as we can produce and can maintain a certain degree of block, not necessarily a complete block. This happens to be a case who is comfortable only when her heart is in complete block. The etiology in this last case I think is rheumatism and tonsillitis causing a valve lesion in the heart, and gradually with the valve lesion there has developed a myocardial disturbance—myocardial insufficiency—and that has gone on for a certain length of time, how long we do not know. The patient had cardiac symptoms ten years ago. In some period in the last ten years her heart ceased to beat regularly and started to be irregular; in other words, auricular fibrillation started with extrasystoles coming in. Just recently she has had a break in compensation and probably that was the time when her heart began to fibrillate. It is in fibrillation now and probably will stay in fibrillation, although she may be made quite comfortable under doses of digitalis to maintain the heart-block.

CHRONIC MYOCARDITIS

October 22, 1917.

DR. CHRISTIAN (to students assigned to cases): I wish you would examine the heart as to size, murmurs, and rhythm, and the pulse as regards tension, volume, rhythm, and condition of the vessel wall.

CASE I

DR. CHRISTIAN (to student): What did you make out (P. B. B. H., Med. No. 7377)?

STUDENT: The heart is enlarged. The apex is in the fifth space, well outside the nipple line. A diffuse apex-beat is seen there.

DR. CHRISTIAN: The heart shows enlargement to percussion out to that point. The right border is 2½ cm. to the right of the midsternal line.

STUDENT: When I first examined the heart the rate was very slow—about 32—but subsequently it increased, and is now 64 at the apex, but occasionally one beat does not come to the wrist. The heart is irregular both in rhythm and in strength. The stronger beat is followed very quickly by a weaker beat which may or may not be felt at the radial. There is a marked systolic murmur best heard at the apex, but heard in the axilla and heard slightly at the aortic and very slightly at the pulmonic areas. The sounds at the pulmonic area are less intense than at the aortic.

DR. CHRISTIAN: What did you take to be the apex-beat? (Indication by student.) Feel a little further out and see if you do not get any. You can get a distinct impulse out further than you have described it—out to where my fingers are; that is, the apex-beat is outside the nipple line. You have got to be very careful in some of these cardiac conditions not to overlook the real position of the apex-beat. Occasionally there will

be apparently a perfectly distinct apex-beat in the normal position, and you take that for the apex-beat and go no further. Then if you go ahead and look out in the axilla you find another beat out there. In other words, a point of vigorous impulse is in about the normal region of the apex-beat, but the ventricle goes further out, and you necessarily feel an impulse out there. You can feel out in the axillary line a distinct apex-beat. The heart is larger than you described it.

STUDENT: I could not percuss the cardiac area satisfactorily.

DR. CHRISTIAN: Sometimes these hearts do not cause any dulness at all if the patient has a good deal of emphysema. It is not always easy to make out definitely the border by percussion, particularly if you percuss rather hard. That is a mistake that is sometimes made by men with longer experience than yourself. They say the heart is of normal size on the basis of finding a perfectly good impulse, normally localized, and do not look further out. This patient has a large heart, but not a very much enlarged heart, however. What would you say about the irregularity?

STUDENT: The beats seem to be grouped. There is a strong beat which will then be followed by a weak one. The sounds are weak.

DR. CHRISTIAN: Are those groups of two or three or any fixed number?

STUDENT: Either two or three.

DR. CHRISTIAN: Yes, there is a distinct tendency to grouping, there being one, two, or three quick beats and then long pauses. There is audible a systolic murmur of moderate intensity. It is heard pretty generally over the precordium, but loudest at the apex. Now look and see how much of an impulse you can see. I think you can see distinctly an impulse at about that point. How about his peripheral vessels?

STUDENT: I do not think they feel particularly sclerosed; they feel soft.

DR. CHRISTIAN: Yes, those are vessels of about normal consistency. The radial is soft. When you roll it under

your finger you can feel it, but it is not particularly thickened. The brachial indicates a little more thickening, but it is not a very abnormal vessel. There is a very moderate degree of sclerosis.

CASE II

DR. CHRISTIAN: We will now take up the next patient (P. B. B. H., Med. No. 7311). What did you make out?

STUDENT: This man's pulse is about 53. His radial artery shows signs of sclerosis—I felt hard masses in it. The tension seems to be rather high. The pulse is of fairly good volume.

DR. CHRISTIAN: There is distinctly an irregular, so-called beaded type of artery. In running your finger up and down you find that it is not very large, but your finger runs over definite irregularities in the vessel where the vessel is thickened, and there are places of about normal consistency. They are not very large vessels. What about his heart?

STUDENT: I find dulness in the nipple line and 3 cm. to the right of the midsternal line. The apex-impulse is of fair intensity about in the nipple line, but you can feel it out well into the axilla.

DR. CHRISTIAN: How far?

STUDENT: Out to the anterior axillary line.

DR. CHRISTIAN: The impulse is a little low. It is not normally placed, but it is only a little outside of the nipple line. What did you hear?

STUDENT: I did not hear any murmurs. The first sound was rather sharp.

DR. CHRISTIAN: The first patient has almost normal peripheral arteries for his age. The second patient has distinctly thickened arteries of the beaded type.

CASE III

DR. CHRISTIAN (to student): Tell us what you found (P. B. B. H., Med. No. 7349).

STUDENT: When I first examined the pulse the rate was about 46, regular and even, but not strong. When I examined it about five minutes later it was beating at about 78, at about

the same strength and regularly. The heart sounds are distant and not very clear. I did not hear any murmurs and the heart did not appear to be enlarged, though it was difficult to make out the apex-beat. The apex-beat is apparently about in the nipple line. The arteries are a trifle sclerosed, not markedly so. The carotid impulse is not marked.

DR. CHRISTIAN: Here again the apex-beat is a little bit further out than described. It is about a fingerbreadth, or possibly a little bit more, outside the nipple line. As you go along with your fingers you feel at about that point practically no impulse, and then inside that quite a definite impulse. In these cases with hearts that are enlarged or dilated the point to take as the apex-beat is the outermost point at which you get a distinct palpable pulsation—not the point at which you get the maximum, because, as I have just said in talking about the other man, sometimes you get the definite impulse 3 or 4 inches inside the left border of the heart. On the other hand, it is not the point furthest out at which you can feel some impulse, because when the enlarged heart pulsates it lifts the chest wall and that lift can be palpated sometimes, particularly with a heart beating forcibly, far beyond what you would say was the left border of the heart as made out by percussion or fluoroscopic examination, so there is a certain personal equation—not the furthest point at which you can feel any impulse, not the point at which you can feel the maximum impulse, but the outer border of a definite impulse. I take it that all three of the gentlemen have tended to underestimate the position of the apex-beat in these cases.

STUDENT: The artery is a little thickened.

DR. CHRISTIAN: It is a little diffusely thickened. The artery in this patient is different from that in the other two. In the first place it is not irregular; in the second place it is a small arterial vessel and as you roll it under your finger there is very definite thickening. As you listen over the heart there is a systolic murmur of very slight intensity and the pulse becomes every now and then regular, and at other times it is irregular. Most of the time when I was listening there it was quite regular. The irregularity when it occurs consists in a weaker beat com-

ing at a shorter interval after the beat of ordinary strength. Did you get any period when you were feeling or listening when there was definite irregularity?

STUDENT: I think the rate was 46 when I first counted it, and then 78. I did not get any transition between the periods.

DR. CHRISTIAN: Keep feeling the pulse and you may catch an irregularity. Most of the time it is regular.

CASE IV

DR. CHRISTIAN (to student): What did you make out in the patient's pulse (P. B. B. H., Med. No. 7394)?

STUDENT: The pulse was irregular at about 85 to 90 per minute. The irregularity consisted in dropped beats. These occurred most frequently once in five, with once in thirty-five as the least frequent. The pulse in general is not very full in volume nor very strong in intensity. The arteries seemed normal.

DR. CHRISTIAN: The arteries are essentially normal ones. They are of normal size, normal volume, and normal tension, and do not roll under your finger any more than you would expect to feel the radial artery.

STUDENT: Very occasionally one of the beats seemed to be longer than those either preceding or following it.

DR. CHRISTIAN: Where did you locate the left border and the apex?

STUDENT: I located the left border 14 cm. from the midsternal line. The apex-beat is rather diffuse. It takes in an area way down here, and when he happens to be sitting just right you can see it down as far as the epigastrium. It is most marked 10 cm. from the midsternal line and a little inside the nipple line, but the cardiac impulse can be felt very distinctly about 14 cm.

DR. CHRISTIAN: What did you hear?

STUDENT: The sounds are not very audible; particularly those at the base. At the apex you get a very distinct systolic murmur taking up the whole of systole. This is transmitted to the axilla and really to the posterior border of the axilla, but

it becomes very faint by the time you trace it that far. At the apex the second sound is distinctly louder than the first. The sounds over the aortic area are quite indistinct. Here, I think, there is a little systolic murmur, probably the same that is heard over the apex area, and the aortic second sound was not very easily heard. Over the pulmonic area the pulmonic second was distinctly louder than the aortic second. The patient breathes pretty largely with the left lung, I should judge, and the noise of respiration tends to obscure the sounds at the base.

DR. CHRISTIAN: Which sound did you say was the loudest at the apex?

STUDENT: The second sound was louder than the first, particularly listening over this area. Neither sound was very loud.

DR. CHRISTIAN: You see the first sound is very largely obscured by the murmur. You can hardly hear the first sound. It is almost replaced by the systolic murmur. You did hear quite distinctly the second sound. The second sound is of normal quality and the first sound is very largely lost. Neither one of the sounds are loud, however, either at the apex or at the base.

STUDENT: The last sound before the skipped beat is louder than the others. I do not know whether that is the interpretation that I give it or whether it is really so.

DR. CHRISTIAN: Very often the sounds when a beat drops out are of different intensity. While I was listening none dropped out, so I cannot say whether there was any change in sounds or not.

CASE V

DR. CHRISTIAN (to student): Tell us what you make out in this patient (P. B. B. H., Med. No. 7282).

STUDENT: His pulse is regular—68 to the minute. There seems to be considerable tension and the artery is tortuous and fibrous, but does not feel calcified.

DR. CHRISTIAN: It is distinctly thickened, is tortuous, but is pretty smooth. Then in regard to his apex?

STUDENT: You can feel the impulse and see it way out into

the axilla. It is about 14 cm., I should think, from the midline—you have to chase it around the corner.

DR. CHRISTIAN: Yes, the impulse goes around the corner—his chest goes out and then almost turns at right angles. You can feel a big impulse out in the axilla. Where you locate the apex-beat by percussion depends on at what angle you percuss and how you percuss. Here is a rounded chest wall, and the heart is in pretty close contact with the chest wall until you get far back. If you percuss at right angles to the chest wall in the axilla you percuss out the posterior border of the heart. If you percuss in an anteroposterior direction you percuss out the left border of the heart more accurately, but practically the heart goes as far to the left as the chest wall goes. In other words, with that shaped chest and a heart that large, percussion gives you a pretty imperfcet idea of increase or decrease in the size of the heart, and I guess if six or eight of us located that left border we would all locate it differently. The essential point is that it is a much enlarged heart, so much so that the left border is out in the axillary region. That is just the kind of a heart that you cannot measure the size of. It may get larger and not change much in position. Already it has gone out to the left in the lateral position as far as it can go. If it gets larger it will occupy more and more of the pulmonary space. It will spread more to the back and then more to the right.

DR. CHRISTIAN (to student): What did you hear?

STUDENT: The second sound is heard loudest at the apex. There are no murmurs. Twice I detected, or thought I did, an irregularity. A^2 is about like P^2 at the base.

DR. CHRISTIAN: Here we are dealing with a heart much enlarged, a patient with peripheral arteriosclerosis as evidenced by tortuosity and uniform thickening of the vessels. Notwithstanding the large size of the heart there is almost no murmur audible anywhere. There is a little bit of a systolic blow at the apex. It is essentially a heart without murmurs, there being just this slight blowing systolic murmur.

CASE VI

DR. CHRISTIAN (to student): Tell us what you made out in your patient (P. B. B. H., Med. No. 7358).

STUDENT: The pulse is beating at the rate of about 90 and has not a very great volume. The arterial wall is moderately hardened.

DR. CHRISTIAN: Is it smooth, or uniform, or irregular?

STUDENT: It is smooth.

DR. CHRISTIAN: Yes, here is another case in which the vessel is thickened—the radial artery—but it is uniformly thickened. It is not particularly tortuous, not as much changed as the preceding man's. How about the size of his heart?

STUDENT: The heart is considerably enlarged. On inspection the impulse is seen in the fifth or sixth interspace possibly. On palpation I think I felt it most prominently in the fifth interspace. It can also be felt in the sixth. On percussion the heart is about an inch or so outside the nipple line.

DR. CHRISTIAN: Here again it is somewhat as in the preceding patient, the apex-beat has gone well out toward the axilla, not as far as in the preceding case, but well out. The impulse is very diffuse, so it is a little hard to say just what you would call the outer border of the apex-beat, but it is well out and certainly out as far as the anterior axillary line. What else did you make out on percussion and auscultation?

STUDENT: The heart is slightly enlarged to the right also. The cardiohepatic angle is acute. On auscultation there is a presystolic murmur and a reduplicated second sound followed by a short diastolic murmur.

DR. CHRISTIAN: Yes, that is present and there is a little thrill with the presystolic murmur. The heart is enlarged and there are some signs of sclerosis and some signs of valve lesions.

CASE VII

DR. CHRISTIAN (to student): What did you make out in your patient (P. B. B. H., Med. No. 7407)?

STUDENT: The pulse is between 60 and 70, irregular at times

and regular at other times. The irregularity seems to bring in more weaker beats. The tension is not very high.

DR. CHRISTIAN: Is the wall thickened?

STUDENT: The wall, I should say, is a little thicker than normal, but not markedly thickened.

DR. CHRISTIAN: Did you feel the brachial?

STUDENT: No.

DR. CHRISTIAN: Well, you will notice that the brachial is considerably thickened. Where you usually feel the pulse in this particular patient the vessel is not particularly thickened, but if you run your finger up the vessel to the midarm you find the brachial becomes very distinctly thickened and a little tortuous. The brachial is very considerably thickened there. That happens sometimes when you feel the pulse just at the wrist, whereas the vessel may be markedly thickened higher up. It is always important in feeling vessels to run your fingers up along the vessel, feeling both in the forearm and in the upper arm. You will sometimes miss evidence of considerable sclerosis if you feel the pulse in the usual way. Here there is nothing particularly abnormal about the vessel at the ordinary place of feeling the pulse. Just a little above there is distinct thickening and also a little tortuosity. What did you make out in his cardiac area?

STUDENT: The impulse comes in a large area in about the fifth or sixth interspace, and goes out to the left about 13 or 14 cm.

DR. CHRISTIAN: You have a diffuse impulse occupying a considerable amount of space and coming pretty well out toward the anterior axillary line. What do you hear?

STUDENT: There is a loud blowing systolic murmur heard at the apex, more or less replacing the first sound.

DR. CHRISTIAN: It is a loud blowing systolic murmur, rather high pitched, and you might say it was a little musical. Are there any other murmurs?

STUDENT: No.

DR. CHRISTIAN: The systolic murmur is transmitted to the axilla and also up along the sternum.

DR. CHRISTIAN: I brought over this group of patients because they all illustrate pretty much the same type of cardiac disturbance. I simply brought these men—there are, I guess, nearly as many women on the women's ward illustrating just the same thing—to give you an idea of the frequency of patients with a certain type of cardiac disease. You see most of them are adults approaching middle life. Some are younger, some are older. They are not young people, and as given in their histories the majority of them are people that have not had any history of acute rheumatism. There is an indefinite history in one, a definite history in another—still in most not a typical articular rheumatic type of history. They are all people who have worked pretty hard, and all people, with the possible exception of one or two, that gave a pretty marked alcoholic history. None of them had positive Wassermann reactions—they are all negative. By no means have all of them arteriosclerosis. Some of them have for the average of their age pretty normal peripheral arteries, so that arteriosclerosis is not a common finding. Their symptoms have varied. They represent the various types of cardiac decompensation symptoms that I have referred to. They have different types of shortness of breath, some with pain, some with anginal-like pain. One of the patients has a history of considerable weakness, and that is said to be his most prominent symptom. He had shortness of breath, etc., but there was this story of weakness. In regard to the types of arhythmia, etc., we will speak at the next time. While they are here I would like you to take this opportunity to come down. Do not bother to try to make out the size of the heart, but listen to the sounds. Go from one to the other, and note the different types of muscle sounds and the different types of murmurs. With the exception of the man here, the patients have nothing but varying forms of systolic murmurs. This other patient has a presystolic murmur. Feel the type of pulse, the thickness of the artery, etc.

October 23, 1917.

DR. CHRISTIAN: This afternoon I am going to discuss the cases that I showed yesterday a little bit more in detail than

we had time for then. First I want to run over the main points in the histories and physical examinations of those cases.

CASE I

The first patient (P. B. B. H., Med. No. 7377) was fifty years of age. He did hard, laborious work and drank alcohol to excess. He had pneumonia when he was twenty-one years of age. He had no other acute infectious diseases. Six years ago he had swelling of the feet and shortness of breath. That, however, did not stop him from work. He worked until a week before he came into the hospital. However, for three months he had been very weak and very short of breath. He had edema of the legs and pain in the abdomen. The student who went over him found that he had some irregularity of his heart-rate; found his heart was enlarged, his impulse being out to the left beyond the nipple line, and that his radials were of about normal make-up. There were no definite signs of sclerosis. When the patient came into the hospital he had a moderate increase in his blood-pressure from the point of view of our hypertension cases, $\frac{165}{110}$,[1] and he had a heart which was percussed 14.5 cm. to the left of the midsternal line and 5 cm. to the right. That was on October 10th. On October 13th he was 13 cm. to the left and 5 cm. to the right. His blood-pressure on the 15th had fallen to $\frac{115}{60}$. When he came in he had, I think, essentially what was made out on the examination here as far as symptoms were concerned. He had a loud systolic murmur at the apex transmitted to the axilla, and that is what we made out here in the clinic. There was an audible systolic murmur of moderate intensity heard pretty generally over the precordium and loudest at the apex. In regard to his pulse the rhythm was described as being irregular, and there was a tendency to grouping of the beats, one, two, or three coming close together, then intervals, and another group of one, two, or three quicker beats—no dominating rhythm.

Here is an electrocardiogram (Fig. 88) taken yesterday

[1] The figure above the line is the systolic blood-pressure, the one below is the diastolic blood-pressure.

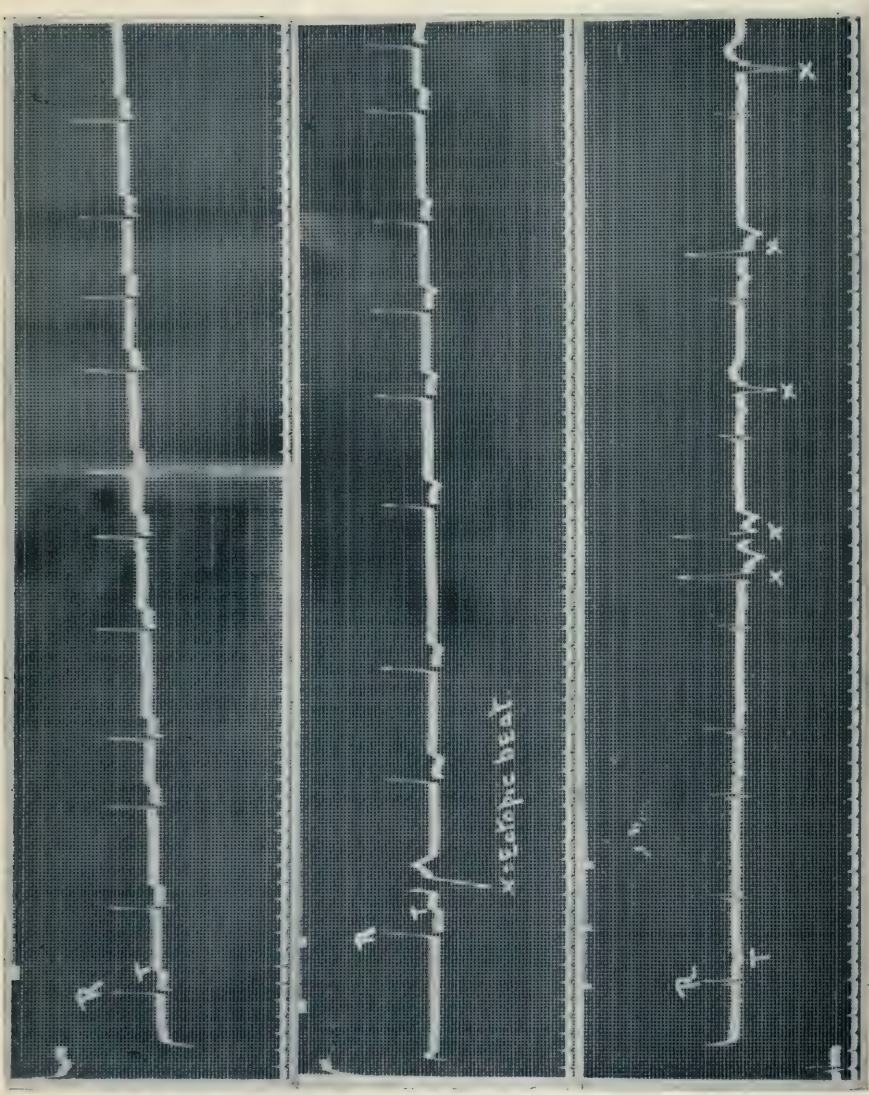

Fig. 88.—Electrocardiograms of Case I, patient No. 7377. *Diagnosis:* Auricular fibrillation; premature ventricular beats from two separate foci. Note the variation in the interval between waves of the type marked *R*, the absence of *P* waves, and at the points marked *X* waves of different forms. These are ectopic beats of ventricular origin and, being of different forms, indicate several foci for their origin.

afternoon after the patient left the clinic, and shows what was described. You will see as it is passed around that there are three beats fairly closely spaced together, then two with longer intervals, then shorter intervals, then longer intervals, and then two shorter ones. They vary in different leads. There is quite a long diastolic pause followed by a little bit shorter one, then two or three quicker beats, and at one point the rhythm is interrupted by an extrasystole. In another lead there are two extrasystoles coming close together of one origin, and then later on there are two or three extrasystoles that start at some other point in the ventricle. One of these starts in the right ventricle and the other starts in the left ventricle. There is no definite muscle preponderance on one side or the other, but the patient has fibrillation, an absolutely irregular pulse, and as you look along the curve there are no signs of definite "P" waves.

CASE II

DR. CHRISTIAN: The next patient (P. B. B. H., Med. No. 7311) is fifty-nine years of age. He was engaged in hard work, drank alcohol to excess. Eight months ago he had some sort of trouble in his feet, not made out to be definitely an attack of rheumatism, and was probably a combination of flat-foot and some edema from his cardiac condition. Apparently he had no fever and it did not involve other joints. It may have been rheumatism, but probably was not. A year ago he began to have shortness of breath on exertion and got dizzy when he stooped over. Nine months before he came in he had a definite attack of cardiac decompensation, swollen legs, distended abdomen, was markedly short of breath, and had nocturnal paroxysms of dyspnea. He got over that attack and was able to work for six months. Three months before he came in he began to get worse, his feet became swollen, his shortness of breath increased, and after about a month he had to cut down largely on the amount of work he did. He began to have nocturnal dyspnea. Two or three times with the dyspnea he had pretty severe pain. The pain radiated down the left arm and into the epigastrium. A small amount of concentrated

urine was passed. That patient, as far as the pulse went, showed quite a marked degree of sclerosis. He was the one with the

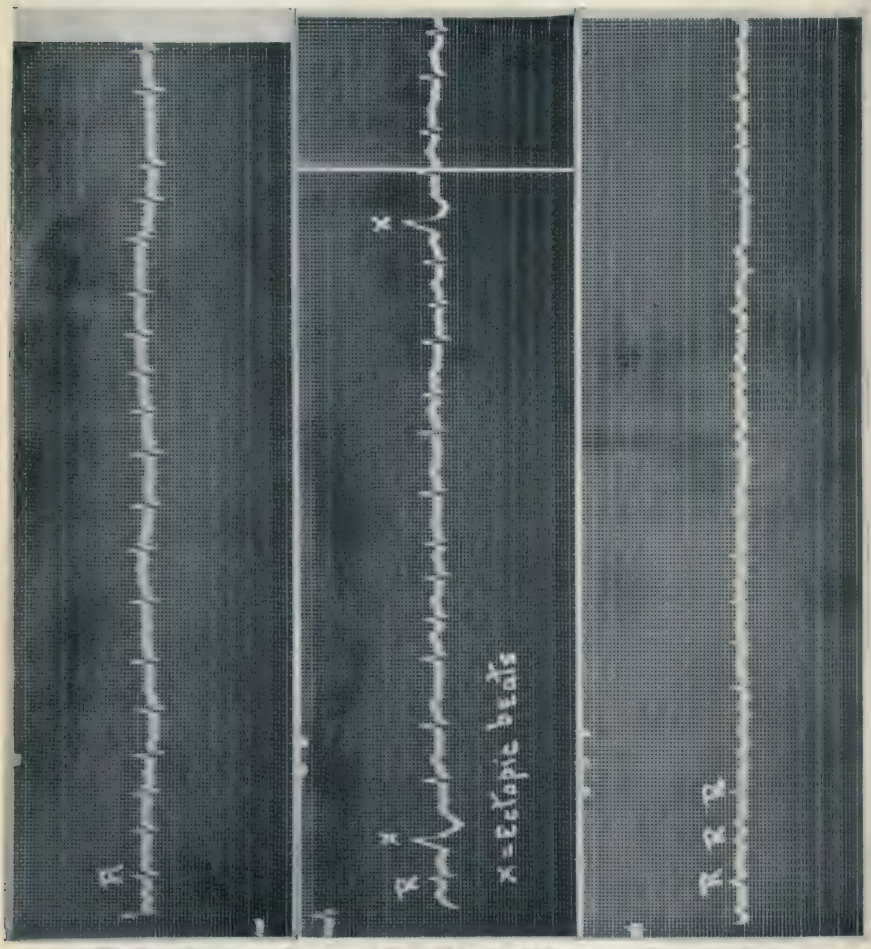

Fig. 89.—Electrocardiogram of Case II, patient No. 7311. *Diagnosis:* Auricular fibrillation; ventricular extrasystoles. Note the irregularity in the rate of recurrence of *R* waves and at the points marked *X* the occurrence of ectopic beats. No *P* waves occur.

small beaded type of artery. He had a cardiac enlargement, the apex being somewhat outside the nipple line. The gentleman who went over him thought he heard occasionally a suggestive

systolic murmur at the apex, but not a very striking murmur; that is, the murmur played a very small part in the physical examination. When he came in he had a blood-pressure of $\frac{170}{100}$. He had cardiac enlargement, the left border being 13.5 cm. to the left and the right border 4 cm., you see not as large a heart quite as the other one, but not very different. That was on the 29th of September. On October 7th the blood-pressure had fallen to $\frac{135}{90}$, cardiac manifestations were essentially the same. That patient's pulse-rate was distinctly irregular, and on studying it we find that, like the other patient, there is absolute irregularity with an occasional extrasystole (Fig. 89). No "P" waves were made out. There was a considerable amount of vibration in the string and only a very occasional extrasystole. You will notice an occasional abnormal beat as the curve is sent around. Again, that is a case of auricular fibrillation.

CASE III

DR. CHRISTIAN: The third patient, the negro (P. B. B. H., Med. 7349), is thirty-six years of age, a moderate user of alcohol, a heavy worker—having worked in a foundry. He had grippe and rheumatism five years ago. That was perfectly typical acute articular rheumatism affecting many joints. Four to five months before he came into the hospital he noticed that he got tired very easily. He got short of breath on very severe exertion. Two months before he came in fatigue was sufficient to interfere with his work, and he found that he could not keep up the pace with the rest of the gang. At work he got very short of breath. After stopping work he did not become very short of breath until about a week before he came to the hospital, and that was accompanied, as he described it, by his being "sick at his stomach." Five days before he came in he himself noticed his heart beating in an irregular fashion. He had, as we went over him, a slight degree of thickening of his arteries uniform in character. He had a moderate degree of diffuse arteriosclerosis. His heart was enlarged to a moderate extent. When he came in on October 5th he had a blood-pressure of $\frac{160}{75}$ and on some days a systolic pressure of only 130. His heart measured 14 cm. to

the left and 3.5 cm. to the right. The first sound was replaced by a blowing systolic murmur heard well out into the axilla. He

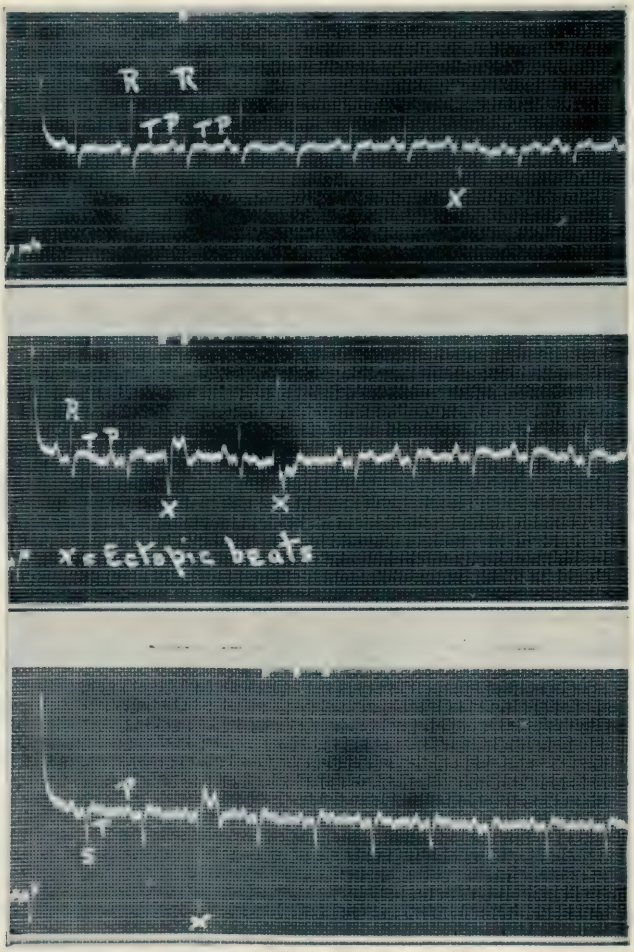

Fig. 90.—Electrocardiogram of Case III, patient No. 7349. *Diagnosis:* Left ventricular hypertrophy; ventricular extrasystoles. The waves of the ventricular complex are indicated by *R* and *T*, and the auricular impulse by *P*. There is a normal relation between the auricles and the ventricles, and at the points marked *X* occur ectopic beats of varying points of origin which interrupt the regular rhythm.

had a definite gallop rhythm to his heart. No other murmurs. On the 11th his heart outline was 5.5 cm. to the right and 13

cm. to the left, and the same harsh systolic murmur was heard. His pulse was, for most of the time, regular. While we were going over him before the class once or twice a small beat was felt shortly after the normal beat. After the class came down and began to go over the patient his pulse became quite irregular and the irregularity consisted in the occurrence of a weaker beat at a shorter point than the normal relation after the regular beats. The electrocardiogram (Fig. 90) confirms that by showing an occasional extrasystole. Otherwise the ryhthm is quite normal and the complex is quite normal as far as the "P," "R," and "T" waves are concerned. That is, the auricle is not in fibrillation, it is beating regularly, and with the exception of the extrasystole the ventricles are in normal response to the stimulus coming down from the auricles. It shows the complex of left ventricuar hypertrophy. This is left preponderance, and in the first lead the main ventricular complex is up and in the third lead it is down, which is characteristic of left ventricular preponderance.

CASE IV

DR. CHRISTIAN: The fourth patient (P. B. B. H., Med. No. 7394) is forty-two years of age. He used alcohol in considerable amount, but not as much as the preceding man. He worked rather hard, but did not do the laborious type of work that the other people did. He was a fruit peddler and, I guess, pushed his cart, and that is not easy work. He had had no acute infections at all. A year before he came into the hospital he woke up suddenly one night with a severe pain in his chest and that pain kept up for about two days. It responded to treatment, and he was all right until eight weeks before his admission, when he again had pain in his chest and shortness of breath. The pain quickly disappeared, but the shortness of breath persisted, and he came into the hospital on account of the shortness of breath, with the added symptom that if he stooped down or exerted himself in any way he had a sensation of pressure in his chest—not actual pain. He had an irregularity consisting of dropped beats, according to the student who went over him, not coming very frequently; once in five, sometimes as infrequent as once

in thirty-five. He had essentially normal arteries. The heart was enlarged, the left border being 14 cm. to the left. He had a diffuse pulsation all over the precordium and down in the epigastrium, and a systolic murmur heard at the apex, transmitted well out to the axilla, etc. He had a blood-pressure of $\frac{125}{90}$ when he came in, and that was on the 14th of October. His heart was percussed 2 cm. to the right and 15 cm. to the left. He had a soft systolic murmur heard over the apex; no other murmurs heard. On October 15th cardiac measurements were 4.5 cm. to the right and 14.5 to the left.

The electrocardiogram (Fig. 91) from this patient shows first a normal relation as far as the auricles and ventricles are concerned, an occasional extrasystole, representing the dropped beat made out by the student that went over the case, and then all of the complexes are abnormal, not having the usual sharp sudden rise and fall. For instance, in the first lead the "R" wave shows a down-stroke and then an up-stroke followed by a down-stroke with a little notch in it. In the second lead it goes up first, then comes down with a notch, and then goes up. In the third lead there is very little departure from the base line. There is an up-stroke, then a down-stroke, then an up-stroke, and the line goes on straight. In normal curves the typical type of "R" wave is first an up-stroke and then a down-stroke, with little interval between the strokes. Here the "R" waves are all abnormal in contour. That represents a type of complex which indicates pretty severe myocardial disturbance. It is the type of change that has been discussed by Dr. Oppenheimer and Dr. Rothschild in the Journal of the American Medical Association August 11, 1917, under the title, "Electrocardiographic Changes Associated with Myocardial Insufficiency, with Especial Reference to Prognosis." It is the type of chronic disturbance in the heart muscle that has a poor prognosis, and, on the whole, that patient as we saw him was the sickest of the group, and in his case there is less probability of much permanent improvement. It is not true, strictly speaking, that he was the sickest looking man, because the next man was probably a little sicker, but the patient that I just referred to is in the hospital for the first

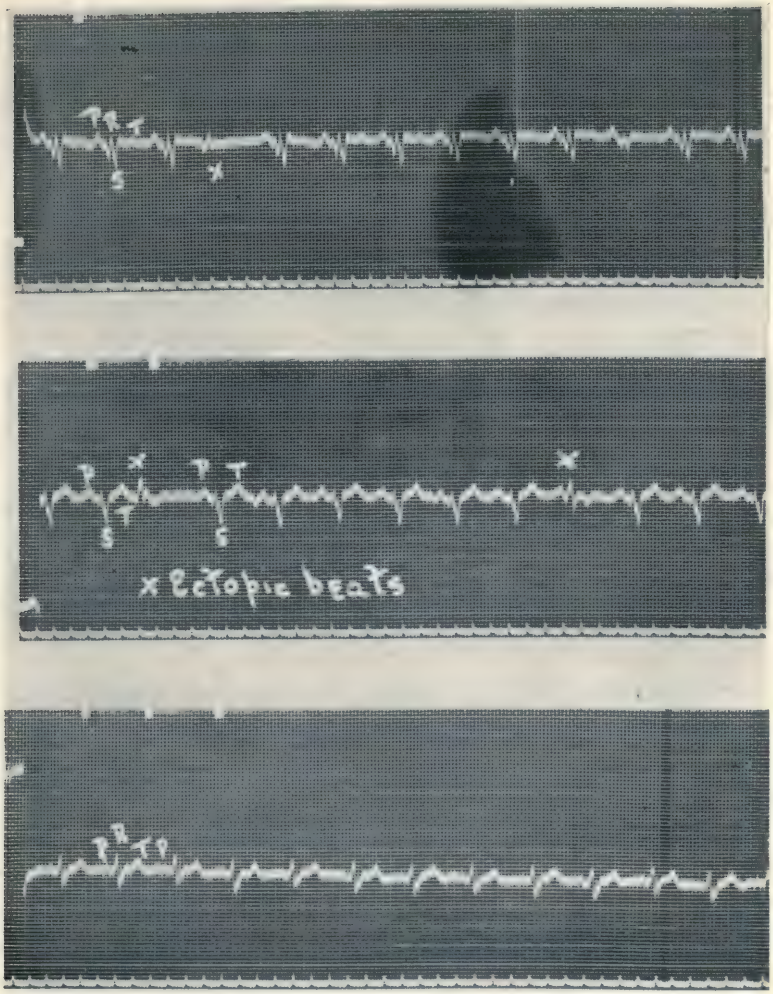

Fig. 91.—Electrocardiogram of Case IV, patient No. 7394. *Diagnosis:* Abnormal form of ventricular complexes; occasional ventricular extrasystoles. *R*, *S*, and *T* indicate ventricular complexes. *P* indicates auricular activity. Note that there is a normal regular relation between auricles and ventricles. At *X* occur ectopic beats. The form of the *R* and *S* waves is abnormal, the line of the wave being thickened and notched, and the interval between its beginning and end being widened, compared with ventricular waves in the electrocardiograms shown in Figs. 88–90.

time, this being his second break in compensation, and the next man is in the hospital for the fifth time, having had about seven

breaks in compensation. In other words, the other man is in pretty bad condition now, but he responded very well to treatment a good many times, whereas this patient will probably not be so satisfactory in that respect.

CASE V

DR. CHRISTIAN: The next patient (P. B. B. H., Med. No. 7282) is sixty years of age. He gives a history of a moderate use of alcohol. However, he worked in a distillery, and the chances are he used more alcohol than two whiskies a day, as given in the history. He did hard labor. He did not sit down and watch the still run. He is a man who did heavy work in the distillery, so there is doubt about his story that he took one or two whiskies a day. He had typhoid in 1911, but no other antecedent diseases. He came to the hospital in July, 1916, with a story that he began to get short of breath fifteen months before that time. Thirteen months before his legs had swelled up. Twelve months before coming he developed nocturnal dyspnea, and that increased so that three months before coming in he started to sleep sitting up in a chair. Three or four months before he came in he had marked swelling of the abdomen. He has been in three or four times since that. He was the man with tortuous, thickened arteries, but not beaded arteries. He had quite marked arteriosclerosis. He was the fellow with the very large heart, going way over into his midaxilla. The feeling was expressed that that heart pretty well filled up that side of the chest, and it was a little hard to distinctly measure its position. Practically no murmur was made out, notwithstanding this very large heart. There was a questionable soft systolic murmur made out at times. As we listened in the clinic we did not hear any murmurs at all. When he came into the hospital this time he had a systolic blood-pressure of 190; diastolic, 130. When he came in his heart was percussed 5 cm. to the right and 20 cm. to the left. His blood-pressure, contrary to the others, has remained high and, in fact, has risen. Here is one reading of $\frac{205}{150}$. No irregularity, I think, was made out. The pulse was regular.

Electrocardiograms (Fig. 92) show a marked left ventricular

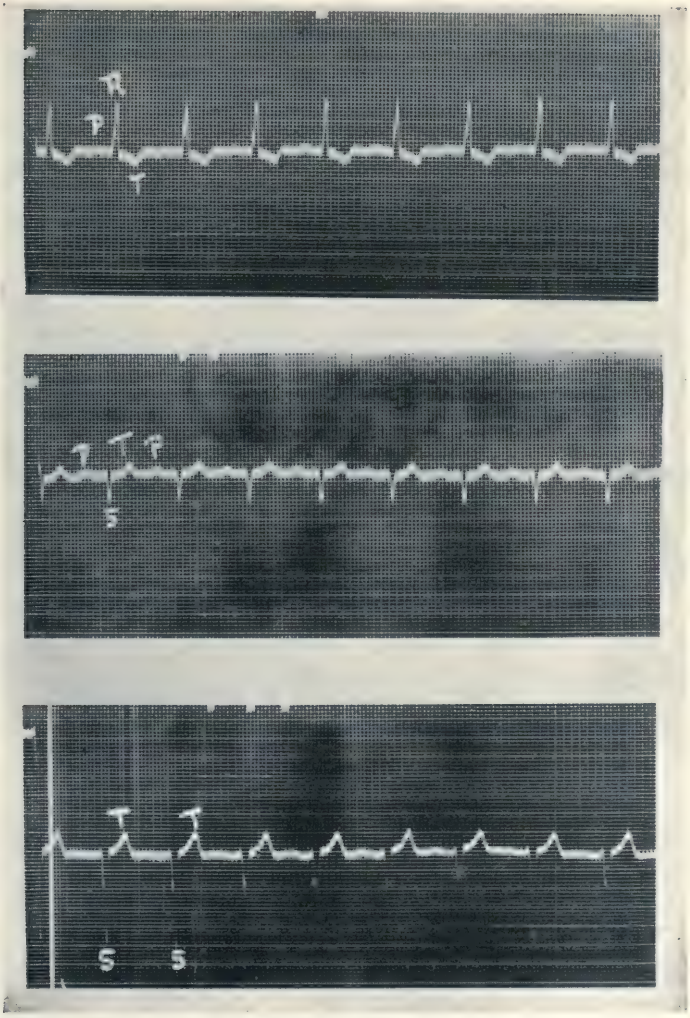

Fig. 92.—Electrocardiogram of Case V, patient No. 7282. *Diagnosis:* Left ventricular hypertrophy. There is a normal relation between the *P* waves, indicating auricular contraction, and the *R* and *S* waves, indicating the beginning of ventricular contraction. The direction of the highest waves in Lead 1 and Lead 3 indicate left ventricular hypertrophy.

preponderance. There are very tall "R" waves in this particular tracing, and a slight irregularity from time to time due to ectopic auricular beats was observed in other electrocardiograms.

The ectopic beats we referred to in previous patients were ventricular in origin. Most of the time the rate is pretty regular.

CASE VII

DR. CHRISTIAN: The sixth patient I will skip over and take up the seventh patient because the sixth patient had a valve lesion, whereas the others did not. The seventh man (P. B. B. H., Med. No. 7407) was fifty-six years of age. He had always been a steady moderate user of alcohol. He had one or two whiskies a day, apparently not more than that, but he kept that up steadily. He did hard, laborious work. He had typical polyarticular rheumatism when sixteen years of age, which was forty years ago. Twelve years ago and three years ago respectively he had the same thing. He came to the hospital for the first time in June, 1916. Three months before that time he began to feel weak, and noticed that his heart pounded. Two months before that he became short of breath. Two weeks before he came in his abdomen became swollen, and three days before coming in his legs became swollen. This is his second admission. Just before he came in this second time he was trying to do light work. Twelve days before he came in he became very short of breath and had palpitation and pain in the abdomen. He had an irregular pulse, a moderate degree of thickening in his radial, and a very considerable degree of thickening in his brachial, artery. He had a loud blowing systolic murmur, at times almost musical. He was fibrillating. Electrocardiograms (Fig. 93) taken in the afternoon show quite marked irregularity, some long pauses, some short pauses—left ventricular hypertrophy and apparently no extrasystole. That case, then, is one of auricular fibrillation. His heart was percussed 3 cm. to the right and 16 cm. to the left. His blood-pressure was slightly up, $\frac{143}{62}$.

CASE VI

DR. CHRISTIAN: The sixth patient (P. B. B. H., Med. No. 7358) was thirty-nine years of age. He had no history of alcohol. He did not do very laborious work, being a cap-maker. There is no history of rheumatism and no history of any acute infec-

tious diseases. Three years before coming to the hospital he had swelling of his hands, feet, and abdomen, apparently an

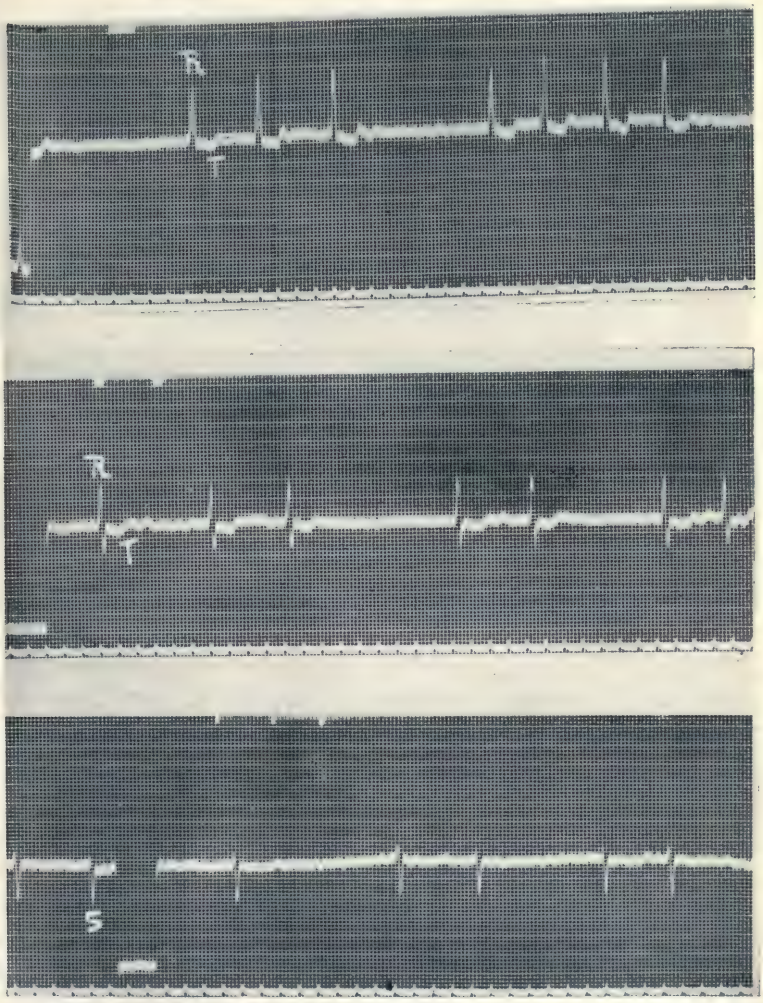

Fig. 93.—Electrocardiogram of Case VII, patient No. 7407. *Diagnosis:* Left ventricular hypertrophy; auricular fibrillation. *R*, *S*, and *T* indicate ventricular activity. *P* waves are absent. In many places the heavy straight line shows slight rapid oscillations, indicating coarser fibrillary contractions of the auricles.

attack of very definite nephritis. About a year before he came in he had a similar attack. His symptoms suggest that he had

a mixture of edema of nephritic origin and edema and shortness of breath of cardiac origin. As we looked him over we found that he had a regular pulse, moderate thickening of the walls, and a very definite presystolic murmur indicating a mitral stenosis. He had a blood-pressure of $\frac{142}{95}$. His heart could not be outlined on account of fluid in his chest obscuring the dulness. The apex was about 14 cm. to the left. He has right-sided preponderance as far as hypertrophy is concerned (Fig. 94); otherwise a normal sequence, regular, no delayed conduction time, and the auricles and ventricles beating in sequence, but a certain tendency toward widening out of his ventricular complexes. It was not marked as in the previous man (Case IV), but rather slower movements of the string than in the preceding case, suggesting a disturbance in the heart muscle.

The point that I wanted to illustrate in these cases is first the varying cardiac symptoms—the different things beginning their symptom complexes—shortness of breath, nocturnal dyspnea, fatigue, pain, edema, etc., as illustrated by these various cases. They also are a group of cases in which, with the exception of one man, there is no evidence of any organic valve lesion. That statement is made, though some of the patients showed no murmur on one extreme, and another patient on the other extreme showed a high-pitched, even musical, harsh systolic murmur at the apex, and the others graded between these extremes, so that there were all sorts of systolic murmurs at the apex as far as localization and quality are concerned, and yet we very strongly feel that none of the patients have a chronic valve lesion. Arteriosclerosis is not a common feature. They illustrate different types of arteriosclerosis and absence of arteriosclerosis, although all have hearts of about the same type. There were beaded arteries, thickened arteries, arteries uniform in diameter, and normal arteries. Arteriosclerosis is not a common feature. Most of them are alcoholic, not all of them. The amount of alcohol varies; some are hard drinkers, some went on sprees, some are moderate continuous drinkers, and some probably used very little alcohol. As I told you before, they all had negative

Wassermann reactions, consequently syphilis did not play any part. All sorts of disturbances in rhythm are illustrated; also

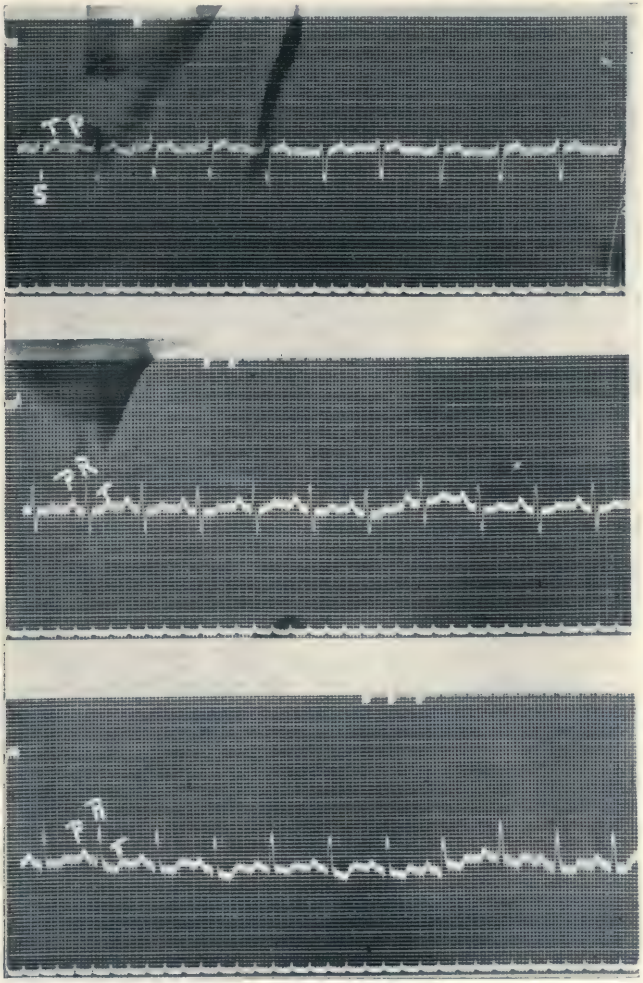

Fig. 94.—Electrocardiogram of Case VI, patient No. 7358. *Diagnosis:* Left ventricular hypertrophy. *P*, *R*, *S*, and *T* waves indicate normal relation between auricles and ventricles. The rate is regular. There is a slight widening in the main curves, *R* and *S* indicating slight myocardial disturbance.

right-sided preponderance, left-sided preponderance, as far as muscle bulk is concerned and an even distribution between the

two sides. That does not mean the heart is not hypertrophied, but means the proportion between the disturbance in the right and left side coincides with the normal ratio as the heart enlarges. Some of them have arhythmias. Some have a regular rate without any disturbance. Some show auricular fibrillation. Some have an irregularity of the extrasystole type; the ectopic beats in one case beginning in the auricles, in two cases beginning in the ventricles. In one in which they began in the ventricles they sometimes began in one place, sometimes in another. Some of them had no disturbance in the electrocardiogram, no disturbance in the rhythm, except muscle preponderance. One of them showed a very distorted type of ventricular complex with a rhythm nearly always regular, occasionally an ectopic beat, but as far as electrocardiograms were concerned showed marked abnormality in the form of the ventricular complex pointing to an extensive muscle disturbance. That was the patient who had quite marked arteriosclerosis and had had two or three severe attacks of pain at night which were interpreted as anginal pain; in other words, coronary arteriosclerosis with rather more signs of organic disturbance in the heart muscle than the other group showed as far as electrocardiograms are concerned.

Then there was the case with all of the manifestations of the other patients as far as weak muscle was concerned, but differing from the others in that he had an organic valve lesion—signs of mitral stenosis. The heart muscle was otherwise in just the same condition as the other group. The reason that I brought him over was because he presents the picture of typical mitral stenosis, but you get no history of any rheumatism, whereas one of the other patients with no signs of a valve lesion had a typical attack of polyarthritis, ordinary articular rheumatism, and one of them had three attacks—one when pretty young and the other two when middle aged, and yet no signs of a valvular lesion. I simply brought those in to contrast them and emphasize the fact that rheumatism may exist and the patient have myocardial disturbance without a valve lesion, but you can find signs of valve lesion without being able to get a history

of rheumatism; in other words, whereas most patients with valvular lesions give a history of rheumatism and most of the cases of myocardial disturbances without valvular lesion do not give a history of rheumastism, there are exceptions. Of course, if you have a patient that suggests a valvular lesion and you do not get a history of rheumatism or infection suggesting rheumatism, that does not justify you in doubting what you hear and what you feel.

Now in regard to these patients from the point of view of what we have done for them and what the results have been. The first patient (P. B. B. H., Med. No. 7377), a fibrillator, came in with a pulse deficit. That is charted on his chart (Fig. 95) by having the apex-rate put down in black circles connected by black lines and the pulse-rate put down in solid black dots connected by black lines. You will remember that the fluid intake and output is represented in the same way. He was given digitalis every two hours for five doses of 0.1 gm. of digitalis. Then he was given 0.1 gm. of digitalis three times a day, and that was powdered leaves, and the leaves grew in Minnesota. (We are using Minnesota digitalis now on the lower floors and Virginia digitalis leaves on the upper floors of the hospital. We are simply trying out some local digitalis, and it is very excellent digitalis. We have used some also from Oregon and some from the State of Washington. It does not seem to make any difference where the digitalis grows in this country, it is really very good digitalis.) As a result of that you will notice that his pulse deficit very largely decreased and he got a diuresis. The urine output jumped from 300 to 1800 c.c. (Fig. 95), and then a few days later went up to 3700 c.c., and in the last day or two it has been about 1500 c.c. on a fluid intake which was restricted to 800 c.c. The patient was on a diet of 800 c.c. of milk, was given digitalis, and the first two nights in the hospital he got morphin sulphate, 15 mgm. the first night and the second night 8 mgm., with 0.5 mgm. of hyoscin; in other words, he got rest in bed, a very restricted diet—800 c.c. of milk—and digitalis, and he has lost over 10 pounds in water as the result of that treatment. He was not weighed the first three days in the hos-

pital. The fourth day in the hospital he weighed 60.7 kilos, and yesterday 55.5 kilos, a loss of approximately 5 kilos, and as there are 2.2 pounds to a kilo, he lost about 11 pounds.

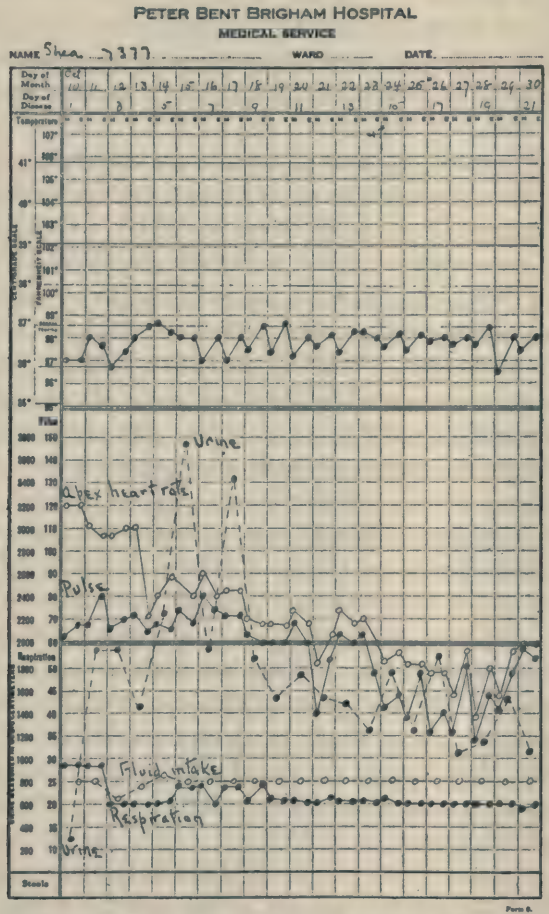

Fig. 95.—Chart of Case 1, patient No. 7377, showing difference between apex heart-rate and radial pulse-rate, so-called pulse deficit. Following the use of digitalis the pulse deficit greatly decreased and there was a marked diuresis.

The next patient's chart (P. B. B. H., Med. No. 7311) (Fig. 96) shows just the same thing. He had a pulse deficit when he first came in with a very rapid radial pulse, and then had a

quieting down of the pulse. His pulse deficit was not so marked when he came in as the other man's. He received digitalis, 0.1 gm. every two hours for six doses, and 0.1 gm. every

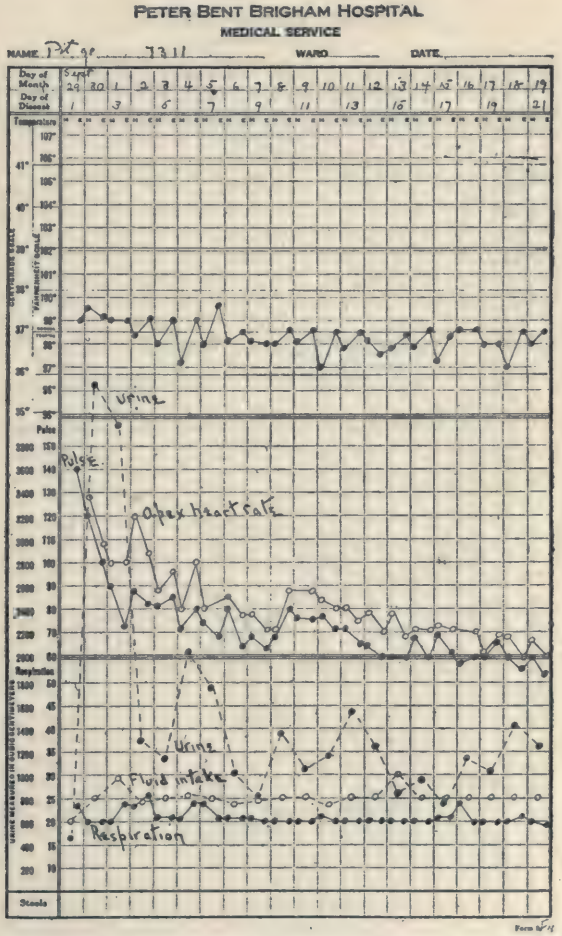

Fig. 96.—Chart of Case 2, patient No. 7311. Here the pulse deficit was less; the radial pulse-rate more rapid. The rate is slowed by digitalis and there is a marked diuresis.

four hours for four doses, then 0.1 gm. three times a day. The first night in the hospital he got codein, 30 mgm., the second night morphin sulphate 15 mgm. One or two nights after that

he was a little restless and got veronal. He was given the same sort of milk diet. After being in the hospital fifteen days he lost 10 kilos, or 22 pounds, in weight, and that was mostly loss of

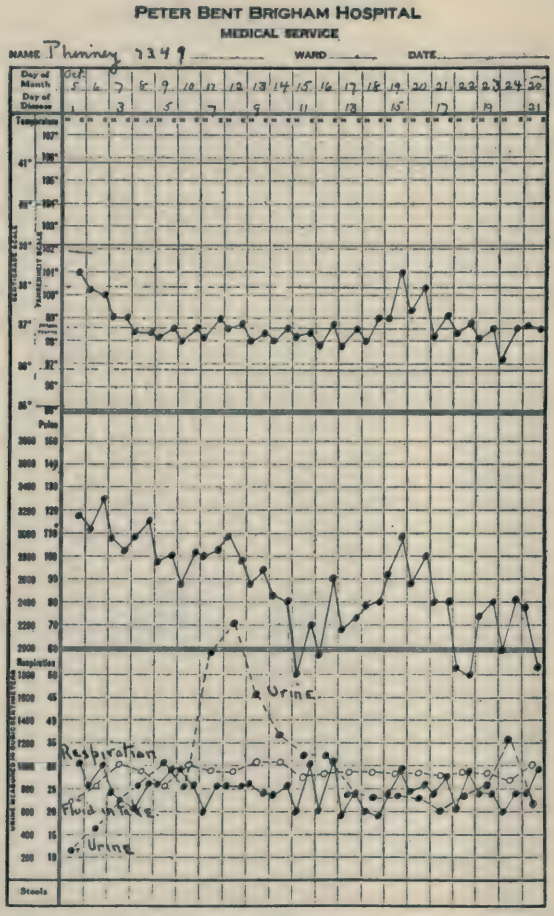

Fig. 97.—Chart of Case 3, patient No. 7349, shows no pulse deficit, but shows slowing of the pulse and a diuresis following digitalis.

water, as he had very active diuresis. Of course there was some loss of flesh on that small amount of milk.

The next patient (P. B. B. H., Med. No. 7349) got digitalis leaves 0.15 gm. every two hours for four doses, and then 0.1 gm.

every four hours for four doses, and that is all he got. He got that in the first two days. That was the patient with extrasystoles. Apparently his extrasystoles seemed to increase and

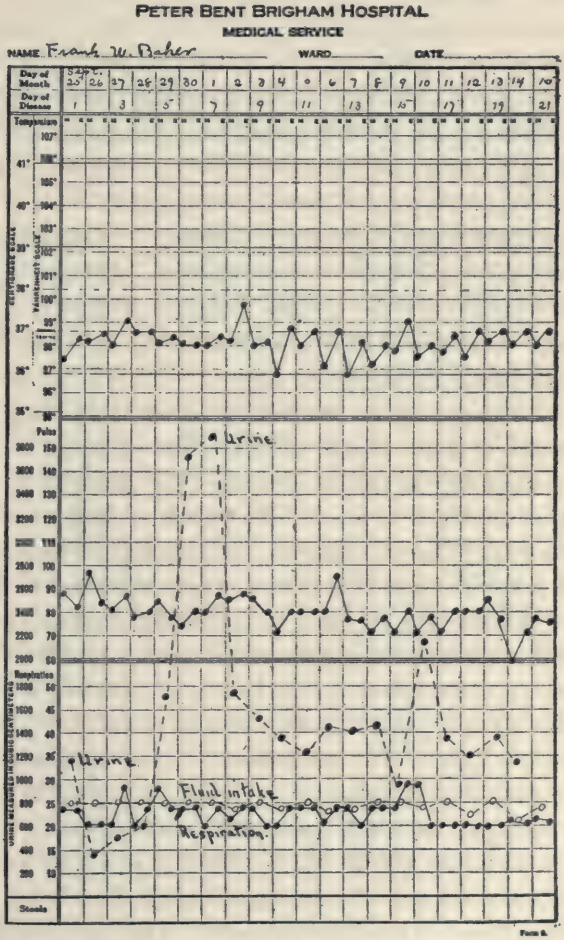

Fig. 98.—Chart of Case 5, patient No. 7282, shows very little change in the pulse-rate, but marked diuresis following digitalis and theocin.

the digitalis was stopped. His pulse is charted (Fig. 97) as 120 when he came in. There was no pulse deficit. It gradually slowed down to about 50. It then increased in rate and he was given some more digitalis. The first night in the hospital he

was given 15 mgm. of morphin sulphate and none subsequently. He did not have very much edema when he first came in, but he lost 7 kilos in weight.

The next patient (P. B. B. H., Med. No. 7394) got a very small amount of digitalis, 0.1 gm. every two hours for four doses. He was given morphin sulphate on two nights, but did not get any more digitalis. He is the patient who had the history of sticking pain in his chest, only moderate edema, and shortness of breath. He essentially got rest in bed for his treatment and only a very small amount of digitalis.

The next patient (P. B. B. H., Med. No. 7282) was started on digitalis about like the other patients. He got diuresis as the other patients have. He got rather a strikingly sharp diuresis, which was added to by using theophyllin or theocin, giving 0.3 gm. and giving three doses. You will notice on this chart (Fig. 98) as it goes around that there is a very considerable diuresis at that point. Before that diuresis he weighed 88.4 kilos, and, as you see, he lost in a short space of time a very considerable amount of fluid. We speak of him as one of our good diuresers. The first time in the hospital on that treatment he lost 39 pounds. The next time he came in he lost 64.6 pounds. He comes in water-logged, and with rest and digitalis, sometimes using a diuretic and sometimes not, he very rapidly floods out his urine. As I said above, that has happened five or six times. He usually gives a pretty prompt response and gets pretty well free from his fluid. The maximum that he has ever lost has been 64.6 pounds and he lost that in ten days, so you see he was pretty busy so far as his kidneys were concerned.

The last patient (P. B. B. H., Med. No. 7407) was treated in just the same way. He was given digitalis leaves, 0.15 gm. at 8 and 10 P. M. This was cut down to 0.1 gm. three times a day, with a gradual decrease in the pulse deficit, marked diuresis, and slowing of the pulse-rate. His weight dropped from 61.4 to 56 kilos in five days.

The case with the valvular lesion (P. B. B. H., Med. No. 7358) was treated just the same way. He had a very considerable diuresis. He was not weighed when he first came in because

he was very dyspneic. He required a good deal of morphin. He is the patient who had a great deal of fluid in his chest. On October 8th he was tapped and 1900 c.c. of fluid was obtained; on the next day 1700 c.c. and on the 13th 1700 c.c., so you see there are 5.3 liters of fluid that were drawn from his chest in three tappings on the 8th, 9th, and 13th respectively. One or two of the other patients, I do not remember just which ones, had fluid in their chests in considerable amount, and that was removed by tapping, so in these cardiac cases if there is a considerable amount of fluid in the chest, so that it seems to be a considerable source of embarrassment, that is removed mechanically. The same thing applies to fluid in the abdomen. We did not tap the patient P. B. B. H., Med. No. 7282, because we were familiar with his habits. We knew that under ordinary circumstances he could get rid of his fluid by action of the digitalis and added to that a diuretic.

What is the etiology in cases of this type? They are almost all alcoholics, but that is probably not the cause of the cardiac lesion. The reason for saying that is we see a lot of these cases that have not been users of alcohol at all, and otherwise they are just the same. Antecedent acute infections probably play a part; some of them undoubtedly. The man with rheumatism probably got his lesion started from rheumatism. Another one had had typhoid fever. That may have played a part, though we do not often see typhoid cause disturbances. Another patient in this group had had pneumonia. We have a case perfectly analogous to this one in the wards now whom I did not bring over because he was so very sick. I did not think it was good judgment to transport him to the clinic and submit him to a certain amount of fatigue when he was so ill. He was in this hospital a year ago with pneumonia. The pneumonia was treated with serum, the temperature promptly fell. His heart was normal in size at that time. His heart was fast when he had fever with the pneumonia, but when he had his crisis it came to normal. We never had any reason to fear the outcome in the case, as we watched him on account of any indications of circulatory embarrassment. That patient has come back in

about a year with a typical story that in the last two or three months he has developed dyspnea; that increased, and he comes in with the picture of a very marked myocarditis, marked cardiac insufficiency, which has not responded to treatment at all. He has been in here for some time and is no better now than when he came in. I do not know that that cardiac lesion is due to pneumonia, but it seems pretty probable that it may be. It just happens that we observed the pneumonia and know that at that time, as far as detected, his heart was normal. We see him again in about twelve months or a little less with a very much enlarged heart, with electrocardiograms indicating this type of thing which we have learned to consider very suggestive of extensive organic disturbance in the heart muscle, so acute infections may play a part, but some of these people did not have acute infections and got the same thing.

Syphilis is so often regarded as the cause of most anything we discuss that it is quite striking that of this group none have syphilis. I did not know that they all had negative Wassermanns until I had them picked out to have sent over, and then found there was not a positive Wassermann in the group. That is in accord with our experience here. Myocardial lesions in the heart as we have seen them less frequently have positive Wassermanns than the average of our patients. The percentage of positive Wassermanns in our chronic myocardial cases is distinctly less than the average of our ward population. That does not say that syphilis does not cause myocardial lesions. It is saying that we see frequently myocardial lesions in which there is no evidence of syphilitic infection. That seems strange if you stop to think that syphilis more commonly than almost any other condition produces vascular lesions. If you go back to your memories of pathologic histology you will recall that characteristic of syphilitic lesions are endarteritis and periarteritis, and you look for extensive vascular lesions as suggesting syphilis. Syphilis is the cause of most aneurysms, another vascular lesion, and yet syphilis does not seem very often to be a cause of chronic myocarditis. We often find in the books just the opposite statement. You find teachers that teach just the

opposite. Dr. Warthin, of Ann Arbor, Michigan, thinks that many myocardial lesions are of syphilitic origin. He has described a good many lesions histologically in the heart as syphilitic lesions. He has stained spirochetes in a good many types of cardiac lesions, but the fact remains that we see many cases of myocarditis in which the Wassermann reaction is negative. It seems to us that syphilis does not play a very large part as a causative factor in these myocardial lesions.

November 6, 1917.

DR. CHRISTIAN: At one of the clinics I showed a group of cases of myocarditis and said that some time I would discuss a little bit more in detail the etiology and the pathology of the lesion in those cases. It is a condition not very well understood from the point of view of etiology. Various things seem to affect the heart muscle and we see a great many cases with these hypertrophied, poorly functioning hearts without valve lesion which at autopsy show really very little that is pathologic in the heart muscle. It has always been a question why that type of heart fails to do its work. It is a big bulk of muscle and often histologically it is pretty normal muscle, and yet clinically we have these marked signs of cardiac inefficiency and symptoms such as shown by that group of patients that I brought into the clinic.

Histologically if you study those hearts, in a certain number you find various kinds of degenerative changes in the heart muscle. Fatty degeneration is fairly common; some of them have hyaline changes in the heart muscle; another group show fragmentation of one kind or another of the fibrils or of the muscle cells themselves. As to that last it is always a question as to how much that is an antemortem and how much it is a postmortem affect and how far it is produced by the technic of hardening and cutting the sections, but some of those cases seem to show very definite destructive changes in the complex fibrils in the heart muscle cells when the fibrils are appropriately stained.

The great trouble in correlating those degenerative changes

with the evident clinical signs of cardiac decompensation lies in the fact that so often at autopsy you get those same kind of changes in patients who during life did not have any evidence of cardiac decompensation. Take, for instance, cases of pernicious anemia. Pernicious anemia usually shows a heart with a marked degree of fatty degeneration, and yet a rather striking feature of pernicious anemia is that cardiac compensation is very good. They may get short of breath with marked anemia, but they do not have signs of cardiac failure, so that these fatty changes can exist without there being much disturbance in the heart muscle function.

In many of these cases we find evidences of circulatory disturbances of the heart muscle; that is, we find changes in the coronaries of a sclerotic type which point to interference with the circulation, but some of those cases, such as the patient with a very large heart whose autopsy material we demonstrated recently, show practically normal coronary vessels—there is no coronary sclerosis. As far as the larger vessels are concerned there is no evidence of poor circulation to the heart muscle.

The question has been discussed a good deal as to whether or not a hypertrophied heart can be a normally functioning heart. That brings up the much discussed question of the athlete's heart; first, as to whether there is any such thing as athlete's heart: and, second, whether an athlete with a hypertrophied heart has not a heart already functionally below par. There is evidence on both sides of the question, both clinical observations and experimental evidence. The fact remains that most hearts larger than normal are hearts not capable of doing the normal amount of work. That is not true of biceps muscle, but seems to be true of cardiac muscle. There may be a circulatory relation there. Cardiac muscle hypertrophies not by a multiplication of muscle fibrils, but by an increase in the size of the individual fibrils. The question has never been very carefully worked out, but the evidence generally goes to show that with the increase in the heart muscle there is not very much of an increase in the capillaries supplying the muscles; or, to put it another way, you have a larger bulk of muscle supplied by pro-

portionately not quite so extensive a capillary system. The enlarged muscle fibrils are surrounded by capillaries, but the functionating part of the muscle substance is further removed from the capillary circulation than occurs when the heart is normal. It would seem probable if under those circumstances the hypertrophied heart muscle, which is continuously working and has only the very briefest period for rest, has less circulation proportionately through it, substances created by the activity of the heart muscle, that is, the waste products, probably would not be removed so rapidly, and in this sense hypertrophy in itself may interfere enough in that broad way with the circulation to make a hypertrophied heart always an inefficient heart, and the simple fact that it has hypertrophied, whatever the cause of the hypertrophy, brings about a deficient cardiac function.

Some of those hearts hypertrophy on account of the in-increased work put upon them by valve lesions, by pericardial adhesions, by peripheral vascular hypertension and causes of that type, and it does not seem so very difficult to understand why these changes might lead first to hypertrophy and then gradual loss of function in the heart muscle. Then there are certain toxic elements that play a part. For instance, the patient who has hyperthyroidism always has an increased heart action as the result of the hyperthyroidism. You are perfectly familiar with the rapid pulse and the palpitation of the heart in the typical case of exophthalmic goiter or hyperthyroidism. Many of those cases, if the hyperthyroidism continues, change their cardiac picture from one of simple tachycardia with possibly slight enlargement to a picture of definite chronic myocarditis with myocardial insufficiency. Very many of the long-standing cases of hyperthyroidism show chronic cardiac failure, so that there we have probably a direct toxic effect on the heart, either as the result of the increased rate and subsequent fatigue or as the result of some direct action on the heart muscle of toxic substances.

Syphilis may explain some of these cases. Syphilis, as I have already said, commonly produces arterial lesions. Syphilis may cause coronary lesions in some of those cases and in that

way lead to damage of the heart muscle. Then the syphilitic lesion itself may produce degenerative changes in the muscle cells, and the degenerated heart muscle cells may be replaced by connective tissue, but then, as I have already said, a very considerable part of these patients with chronic myocarditis have no evidence of syphilis and syphilis cannot be made responsible for the bulk of the cases. It is possible that in a few cases antecedent infectious diseases of one kind or another or simple infections may start a toxic degenerative process in the heart muscle, and that subsequently continue into a chronic myocardial lesion. That apparently is not very frequent because we so often see patients who have gone through pneumonia, typhoid fever, scarlet fever, and infections of that type, and subsequently they have practically no signs of cardiac damage. Occasionally we see patients who following some sort of infectious disease do develop myocarditis such as the patient in the ward to whom I referred as having developed myocarditis within a year following an attack of pneumonia. It is possible there that the pneumonia was the direct cause of the myocardial lesion.

Since the pathologist at autopsy so often can find no lesion to explain why the heart is enlarged, why the heart has failed, various men have tackled the problem from different points of view and made an effort to explain how slight lesions found in the heart muscle conceivably might cause the deficient function. One of the early workers in that field was Krehl, who was at that time in Leipzig, and the work is ordinarily spoken of as the work of the Leipzig School. Krehl and a group of his associates in the Department of Medicine there (Krehl was an internist, not a pathologist) studied large numbers of hearts by taking blocks of tissue systematically from different portions and sectioning them, and found very commonly in those hearts whereas there was not much connective-tissue increase in many of the blocks, yet if the heart muscle was studied *in extenso* you found numerous areas of connective-tissue increase, and he rather thought that the bulk of that process represented enough mechanical interference with the action of the heart muscle by

the connective tissue to explain fairly well the hypertrophy and the subsequent failure of function. Occasionally we see patients in which there is no question but that a chronic diffuse interstitial myocarditis with connective-tissue increase all over the heart muscle is directly responsible for the inefficiency of the heart muscle, but those cases are not very common. At autopsy every now and then we see one of that type. The characteristic thing is that usually there is relatively little connective-tissue increase and that is focal in its distribution.

Krehl and some of his associates had the idea that probably masses of connective tissue not very large in themselves might be situated in certain regions so that they would definitely interfere with the heart function, and that group of men rather worked out the idea that the muscle groups that controlled the heart valves, in part the sphincters, in part the groups of muscle masses to which the chorda tendineæ are attached, might have a more definite function than we ordinarily think of, and slight damage in these particular places might interfere enough with the function to give you regurgitation, and subsequent to the regurgitation back-pressure and a train of disturbances more or less mechanical after they were started. That was the general viewpoint of Krehl and the Leipzig School, that the thing could be explained on the basis of small areas of connective tissue interfering in some way with the function of the heart. That idea was elaborated a little bit more by a man named Albrecht, who published a very extensive monograph on the heart muscle (Der Herzmuskel und seine Bedeutung f. Physiologie, Pathologie und Klinik des Herzens, Berlin, 1903), which I will pass around, and which boils down to the viewpoint that the heart muscle should be regarded in the same light as any other muscle in the body; namely, a complex structure with muscle bands or muscles with tendons that had definite points of insertion and definite points of origin, and that the ventricles, for example, were not simply masses of muscle without any particular structure, but highly organized muscle in the sense of muscle groups whose function depended upon a particular interrelation and correlation as they contracted and as they relaxed, and in that

sense slight disturbance placed at certain points, which might easily escape detection unless very careful study was made of the entire heart muscle, might be responsible for very extensive disturbance in the function of the heart. Of course there is a certain amount of reasonableness in that viewpoint, but it has not been very generally accepted and not very many people have agreed with Albrecht in that view.

When Aschoff and Tawara took up the study of the conduction system of the heart and found out how extensive it was, they made an attempt to explain the lack of function on the basis of the distribution of small degenerative processes in the conduction system at different points, explaining the poor function by the interference with the arrival of stimuli, so that they arrived at different parts of the heart at different times; on this account instead of getting perfectly simultaneous stimulation at all parts of the ventricles you get an irregular stimulation and irregular contraction response. Obviously if that happens it considerably interferes with the function. They brought together their views in the study of a certain number of cases in this little monograph which was published in 1906 (Aschoff and Tawara, Die heutige Lehre von den pathologischanatomischen Grundlagen der Herzschwäche, Jena, 1906). It is of interest that what I referred to in regard to the electrocardiographic disturbances that were emphasized recently by Oppenheimer and Rothschild—abnormal ventricular complexes somewhat suggesting a degenerative condition in the right or left branch of the bundle of His—probably do point to an interference with the peripheral distribution of the conduction system, and they found in a considerable number of cases which they studied areas of connective tissue increase along the intraventricular septum, etc., fitting in with the theory of Aschoff and Tawara and the electrocardiographic disturbance pointed to that change. This very recent work with the electrocardiograph rather definitely favors the view of Aschoff and Tawara that the association of the lesions with the conduction system may explain how rather trivial lesions, trivial in the sense of their size as made out by histologic examination, may cause very marked disturbances in the cardiac

mechanism. However, it is to be remembered that only relatively few cases of myocarditis show these abnormal ventricular complexes. It is not at all improbable that all of these factors may play a part.

The point remains that there is a definite form of cardiac decompensation in which there is no valvular lesion and which at autopsy shows precious little pathologic disturbance. During life we call those cases of chronic myocarditis. We have long since learned that that term does not mean that at death we are going to find an extensive interstitial myocardial lesion; sometimes the pathologist will find a lesion, very often he will find none at all, and in that sense it is not a very good name for the condition. It has been in use for a long time, and is, on the whole, about as good as any of the other names suggested, so we have continued to use the term in that sense referring to that particular type of case, realizing that the pathologic diagnosis very often will not conform to that diagnosis, that the pathologist uses myocarditis in the sense of an inflammatory process—a chronic inflammatory process—and that he may or may not find connective-tissue increase, and in the latter event he will not call it chronic myocarditis, and yet during life there has been a chronic disturbance in the function of the heart muscle rather than in the valves or in the peripheral channels. Some of the cases have hypertension and some of them do not.

CLINIC OF DR. ELLIOTT P. JOSLIN

NEW ENGLAND DEACONESS HOSPITAL

TWO CASES OF SEVERE DIABETES[1]

ALTHOUGH you are about to commence practice with a clean slate and a mortality of zero, I venture the prediction that you are destined to spend many anxious hours and many sad ones, too, in an effort to combat the disease which is to claim our attention this afternoon, and the complication which gives to it its chief terror. The increasing prevalence of diabetes you will appreciate when I tell you that it is recognized four times as frequently in Boston today as in 1890, and twice as frequently throughout the registration area of the United States as in 1900. And as for the importance of diabetic coma as the chief complication, my own statistics are a mute but faithful witness. Thus, up to December 1, 1916, 60 per cent. of all my fatal cases of diabetes died of diabetic coma and coma was responsible for 82 per cent. of the mortality of all those cases who succumbed during their first year of the disease, and of all the fatal cases in children save one.

Coma is a complication which is almost always preventable. It occurs in severe diabetes; however, it may develop in a diabetic whose diabetes is of moderate severity, though made artificially severe by accident or improper medical treatment. Most of those cases who die of coma during the first year of the disease undoubtedly belong to this group, and, I regret to say, some of them were under my own care. The distinction between severe diabetes and diabetes accompanied by acidosis should be emphasized. By severe diabetes is generally understood that

[1] The two clinics upon which the data here given are based and at which the patients here described were shown were held at the Peter Bent Brigham Hospital at the invitation of Professor Henry A. Christian in December, 1917.

type of the disease in which the patient excretes sugar in the urine when on an exclusive protein-fat diet, plus, at the most, 10 grams of carbohydrate in the form of green vegetables. The presence of severe diabetes by no means implies the simultaneous presence of acidosis. The 2 cases of diabetes which I shall show you this afternoon showed acidosis at entrance, but before discharge this had disappeared, and yet the diabetes remained severe. As a matter of fact, no cases under my care have ever come so near diabetic coma and then recovered as these. They illustrate well what I have already said, for though the complication has been overcome, the disease in all its severity remains. The ability to make this distinction constitutes a great advance in our diabetic knowledge. But increased knowledge means added responsibility, and I believe one can usually say with truth that for each death by diabetic coma there is some one who should bear the responsibility.

You may well be dismayed, for I have told you that nearly two-thirds of all diabetic patients have succumbed to coma, and in the next breath assert that generally some one is to blame. While this is the case, because before the law there is no excuse for ignorance, on the other hand, some other facts which I will present to you are reassuring. For this reason I will summarize the experience of the Massachusetts General Hospital for a long series of years, as well as my own recent results with private patients at the Corey Hill and New England Deaconess Hospitals, and you will see that the results of treatment are very different now from what they were even a decade ago.

TABLE I

THE RECENT IMPROVEMENT IN DIABETES AS SHOWN BY THE STATISTICS OF THE MASSACHUSETTS GENERAL HOSPITAL

Period.	No. of cases.	Mortality during hospital stay. No. of deaths.	Percentage.
1824–1898	172	47	27
1898–1914	284	80	28
1914	51	8	16
1915	89	11	12
1916	103	8	8
1917	105	6	6

TABLE II

CASES OF DIABETES TREATED AT THE COREY HILL AND NEW ENGLAND DEACONESS HOSPITALS BY E. P. J.

Year.	No. of cases.	Mortality during hospital stay. No. of deaths.	Percentage.
1913	43	4	9
1914	60	3	5
1915	109	6	6
1916	164	8	5
1917	181	4	2

No one inspecting these two tables can fail to see the improvement which has taken place in treatment. The type of patient has not essentially changed, but the character of the treatment has greatly altered, and for the better. And although one cannot say that all of the deaths at the Massachusetts General Hospital were due to coma, most of them were, and the evidence which such a group of statistics furnishes indicates that coma must have become less frequent, and that acidosis, the forerunner of coma, has been better treated. However, I feel confident in assuring you that the end of progress along this line has by no means been reached. Even adopting the same plan of treatment as that which I shall describe to you today, I believe that 3 of the 4 deaths from coma during 1917 in my own hospital series would be avoidable, and I am convinced that it would avail even if applied to patients in a condition still more desperate.

Before asking the patients to come in, may I say a few words about the etiology, diagnosis, and treatment of this condition?

The *cause* of the coma of diabetic patients is due to acid poisoning (acidosis), or now perhaps better and more commonly expressed, to the diminished alkaline reserve of the body. Acidosis can occur in health if the carbohydrate in the diet is excluded, and it will become severe when, along with protein, fat is taken in excess. In diabetes it may also develop under similar conditions when carbohydrate is excluded from the diet, but it will also appear when carbohydrate is taken but not assimilated. In other words, acidosis will appear when the body does not have carbohydrate to burn or suddenly loses the ability to burn it.

Unfortunately, the *symptoms* of the patient do not always suggest the severity of the condition. Even nurses and doctors

who have seen many patients go into coma occasionally overlook the imminence of its onset. Restlessness, weariness, extreme languor, and various forms of indigestion often precede its full development, and, like the crowning symptom of exaggerated breathing (hyperpnea), may pass almost unnoticed. Therefore, I caution you always to see your severe cases frequently, and to be on the watch for anything in symptoms which differs from the usual in the patient's condition. The laboratory helps us out, and by examination of the urine, blood, and respiration a knowledge of the actual condition can be obtained. It is true that analyses of the blood furnish us with the most direct data, and next to these come the tests of the expired air, but even if these rather more complicated methods are not at your disposal, the simple reaction for diacetic acid, made with the aqueous solution of ferric chlorid, will seldom play you false. So far as I am aware none of my diabetic patients have ever developed diabetic coma who did not show a positive reaction for diacetic acid in the urine, and this is the important point. It is true that during diabetic coma this reaction in very, very rare instances disappears, but I remember to have seen this only at such a stage of the coma that the patient was beyond help. I wish to emphasize this point, because no one should endeavor to escape the responsibility for a death from diabetic coma because he is without the modern appliances for the examination of the blood and breath.

The *treatment* of diabetic coma which I employed for about fifteen years was based upon the principle that alkalis were needed to combat the acidosis and, therefore, should be used in large quantities. For this reason I gave enormous doses of alkali—not uncommonly over 100 grams in twenty-four hours. My results were unsatisfactory, and though the alkalis cannot be blamed by any means entirely for the multitude of deaths from diabetic coma which I encountered, yet I believe they played an important part in preventing recovery—indirectly it is true—through the nausea and vomiting which they provoked and the consequent inability of patients to take food or drink. At any rate, during the last few years I have felt far better satisfied with my results from treatment without alkalis, and until re-

turns from other methods of treatment show more success I commend my course to you. I do this notwithstanding the fact that in November you were advised by an eminent authority to give 5 grams of sodium bicarbonate in 100 c.c. of water by mouth every hour, with the suggestion that in case the bicarbonate were not retained, 250 c.c. of a 3 per cent. solution of sodium bicarbonate should be administered intravenously at intervals of three or four hours. I realize that you are in somewhat of a quandary, for "When doctors disagree—," but may I point out that in the one case the treatment was advised, but the results of treatment were not given, whereas I shall report to you the results of treatment and leave the decision to you as to whether to adopt it. But, again, may I emphasize how sorry I should feel if you should infer from anything I have said that I consider present methods satisfactory. They are not. Perhaps most of all they are valuable because they establish a basis on which the usefulness of other methods of treatment may be tested. Just as soon as I find a series of cases of diabetes of greater severity successfully treated in any other manner I shall be only too glad to adopt the procedure. It is for this reason that I have recorded data in Table III regarding 15 of my cases who have been threatened with diabetic coma and left the hospital alive. For your encouragement and mine I would point out that 7 of this series replace 7 cases less severe in a similar table published only six months ago.

Presentation of First Case.—The younger of these two patients I now show you, Case No. 1012, gave a history of polyuria and weariness in January, 1915, at the age of thirteen years, and in the following month the urine was of 1035 specific gravity, contained 5.1 per cent. of sugar, and the acetone and diacetic acid reactions were triple positive (+++). The etiology remains obscure, for obesity, heredity, and a history of recent infections were wanting. At onset the patient weighed 64 pounds, but, as not unusually happens following the discovery of the disease and adjustment of diet, the weight increased 11 pounds in the next seven months—a gain in weight which most clinicians have recently come to regard as inconsistent with safety during

TABLE III

SUCCESSFUL TREATMENT WITHOUT ALKALIS OF 15 CASES OF DIABETES THREATENED WITH COMA

Case No.	Date.	FeCl.	NH_3.	Blood, CO_2 mm. Hg.	Alveolar air, CO_2 mm. Hg.
691	Nov. 15, 1917	+	..	..	20
1200	May 29, 1917	+++	2.3	..	18
786	June 11, 1916	++	3.9	..	18/20
	12,	+	3.2	24	21
765	Dec. 6, 1915	+++	3.3	..	21
	Jan. 24, 1916	++++	2.6	..	21
942	July 12, 1916	+++	4.4	20	20
	13,	++	3.7	..	17
938	Nov. 2, 1917	++++	1.3	..	18
1303	May 30, 1917	++	2.1	..	21
1273	March 30, 1917	++	..	..	22
755	April 15, 1917	+.	1.6	..	18
1011	March 29, 1916	++	1.8	..	23
	April 13,	++	..	..	22/22
	Sept. 25, 1917	++++	..	..	15
1085	Oct. 30, 1916	?	1.7	28	20
1196	Dec. 8, 1916	++++	4.6	..	21
	9,	++	6.0	26	22/14
	10,	+++	3.3	..	18/20
	11,	+	3.1	26	20
	12,	++	3.3	..	21
	13,	++	2.9	..	24
1070	June 23, 1916	++	1.9	21	20
1012	Sept. 13, 1917	+++	..	..	14
	14,	+++	2.5	21.3	14
	15,	++	2.3	..	16
1120	Sept. 6, 1916	+++	..	..	21
	7,	+	..	..	18
	Oct. 11,	++	1.9	..	22
	14,	o	..	..	20
	27,	+	..	..	15

the first year of treatment of the young diabetic. In March, 1916, the patient first came under my observation. Physical examination was negative, save for emaciation and weakness—untoward signs in a child—weight 68 pounds (31 kilograms), height 4 feet $6\frac{1}{2}$ inches. (Today, December 31, 1917, the weight of the patient has decreased 10 pounds, but the height has advanced 3 inches.) An acetone odor to the breath was absent despite the quadruple plus (++++) ferric chlorid reaction in the urine for diacetic acid.

The patient was placed upon a diet containing

	Carbohydrate, grams.	Protein, grams.	Fat, grams.
5 per cent. vegetables (300 grams).....	10	5	0
Small oranges (2).....	20	0	0

for the balance of her first day in the hospital, as well as the succeeding day, but upon the following day the oranges were omitted. Fasting, save for washed vegetables, was carried out the next twenty-four hours and complete fasting for the day following, with the result that the urine became sugar free and the diacetic acid reaction fell to one plus (+). That the acidosis still was important is shown by the 2 grams of ammonia which the urine contained on this day instead of a normal of 0.5 to 1 gram, and this was also confirmed by a lowering of the carbon dioxid tension of the alveolar air from its normal at 40 in terms of mm. Hg. to 29. The significance of these modes of expression of the acidosis has been explained in previous clinics by Dr. Palmer and Dr. Geyelin. I will simply point out here that urinary ammonia values above a gram represent an increase, and that this is nature's method of furnishing an alkali to counteract acidosis. A lowering of the CO_2 in the alveolar air implies a similar lowering of the CO_2 tension in the blood, and is due to the replacement of the normal but weak carbonic acid by the abnormal but strong beta-hydroxybutyric acid and its derivatives.

The day of the washed vegetables upon which the urine became sugar free was followed by a day of complete fasting, and that by a day in which the diet contained 5 per cent. vegetables, 150 grams—the equivalent of 5 grams of carbohydrate and three of protein. (The average of the vegetables in the 5 per cent. group do not show over 3 per cent. carbohydrate, especially after they have been cooked, and I therefore, as a rule of thumb, consider that each 30 grams (1 ounce) of 5 per cent. vegetables contain 1 gram of carbohydrate and ½ gram of protein.) This addition of carbohydrate to the diet brought no return of sugar, and while upon it the diacetic acid reaction disappeared and did not recur up to the time of the discharge of the patient from the hospital May 22, 1915. During this first hospital stay the carbohydrate in the diet was gradually increased to 20 grams, later simultaneously the protein and fat, and glycosuria did not occur for over two weeks, at which time the food amounted to carbohydrate 21 grams, protein 43 grams, fat 40 grams; calories

per kilogram body weight 20. The blood-sugar at this time was 0.21 per cent., unfortunately nearly twice the normal.

The rapid disappearance of the diacetic acid reaction and the return of the CO_2 tension of the alveolar air to normal (38 mm. Hg.) in this case in contrast to the persistence of such reactions in cases apparently not so severe, but under treatment with large doses of sodium bicarbonate, is to me striking and significant. For example, Case No. 344 of my series showed 2.6 grams of ammonia in the urine on June 29, 1910, and from that date until February 26, 1912, constantly was under alkaline treatment. At no time did the urine fail to show a diacetic acid reaction, although sodium bicarbonate, usually 20 grams or more, was ingested daily. Contrast Case No. 344, unsuccessfully taking 6 teaspoonfuls of soda for a period of twenty months, with this little child, achieving freedom from acidosis without any alkali in half as many days. Surely clinicians will hesitate long before adopting the advice of the laboratory expert "that the therapeutic use of soda should be one of the most frequent prescriptions of the physician."

It would be unfair, however, to imply that the only difference in the treatment of acidosis between Case No. 344 and our present patient consisted in the administration of the alkalis to the one and the withholding of the same from the other. There were, in fact, two other radical differences: the first relates to the rôle played by fat in the diet, and the second to fasting—each of fundamental importance in the treatment of acidosis and about each of which little was known in 1912—mark you, only five years ago. In this patient's present chart (Table IV) you may have noted that all fat was withheld from the diet until for some time after she had become sugar and acid free. This is perhaps the crux of the situation, for in the fat of the diet or of the tissues acidosis finds its origin, and it matters little whether the subject is diabetic or not, provided he is either, like the diabetic, unable to assimilate carbohydrate, or in the case of a normal individual, deprived of it. As you will remember, Folin and Denis have beautifully shown that in the first fast of an obese, but otherwise healthy individual, acidosis occurs, though they also showed

TABLE IV

CHART OF CASE NO. 1012

Date.	Diacetic acid.	Ammonia, total gm.	Sugar in urine, gm.	Diet in grams.					Carbohydrate balance, gm.	Weight, kg.	Blood-sugar, per cent.	Alveolar air, CO_2 mm. Hg.
				Carbohydrate.	Protein.	Fat.	Alcohol.	Calories.				
1917												
Sept. 13	+++	0.2	(3.3%)							26		14
" 13–14	+++	2.5	30	20	17	0	0	148	−10		0.36	14
" 14–15	++	2.3	34	15	3	0	0	72	−19			16
" 15–16	+		22	10	3	0	0	52	−12	26		16
" 16–17	++		18	0	0	0	0	0	−18			20
" 17–18	+		19	0	0	0	0	0	−19			29
" 18–19	sl. +		25	5	24	0	0	128	−20			23
" 19–20	sl. +		13	5	24	0	0	128	− 8	27		19
" 20–21	+		22	5	24	0	0	128	−17			19
" 21–22	sl. +		11	0	0	0	0	0	−11			
" 22–23	sl. +		4	3	18	0	8	140	− 1	28		19
" 23–24	+		11	0	0	0	15	105	−11			23
" 24–25	+	2.6	21	0	24	0	15	201	−21	29		19
" 25–26	0		10	0	0	0	15	105	−10		0.31	21
" 26–27	sl. +		0	0	0	0	15	105	0			23
" 27–28	0		0	0	0	0	15	105	0			23
" 28–29	0		5	0	24	12	15	319	− 5	30		22
" 29–30	0		5	0	24	24	15	417	− 5	31		28
Oct.												
" 30– 1	0		9	0	24	24	15	417	− 9	32		26
Oct. 1– 2	0		8	0	24	24	20	452	− 8	33		30
" 2– 3	0		0	0	0	0	0	140	0		0.26	27
" 3– 4	0		3	0	24	24	20	452	− 3	32		
" 4– 5	0		5	0	24	24	20	452	− 5			
" 5– 6	0		9	0	36	32	20	572	− 9			
" 6– 7	0		10	0	36	40	20	644	−10			31
" 7– 8	0		12	0	36	40	20	644	−12			
" 8– 9	0		4	0	0	0	20	140	− 4			28
" 9–10	0		0	0	6	6	15	183	0	30		
" 10–11	0		0	0	12	12	15	261	0		0.24	

that this appeared less severe during subsequent fasting periods. The lesson of our case and that of other similar cases has so strongly impressed itself upon me that it has led me to suggest the following preparatory treatment for fasting in all cases of diabetes with acidosis and in some other groups as well, when an acidosis if it did develop might become serious because of cardiorenal complications:

In severe, long-standing, complicated, obese, and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat; after two days omit

protein, and then halve the carbohydrates daily until the patient is taking only 10 grams; then fast. In other cases begin fasting at once.

Fasting during two days was the second element in addition to the omission of fat, which hastened the rapid disappearance of the acidosis in our little patient. Allen has clearly pointed out that fasting usually leads to the disappearance of acidosis in the diabetic, though occasionally, as Stillman, working with him, has shown, this does not occur.

The patient left the hospital on May 22, 1916, free from acidosis and sugar, with a blood-sugar of 0.13 per cent. and a diet containing 34 grams of carbohydrate, 72 of protein, and 113 of fat, 1441 calories. She weighed 67 pounds (30.5 kilograms). Today, nearly two years later, I feel I made a mistake in allowing so large a diet, for you will note that the patient was receiving approximately 50 calories per kilo, whereas undoubtedly 40 calories or even less would have sufficed, and, as I hinted above, would have been far safer.

I am partly led to this opinion because on December 22d the patient returned to the hospital weighing 69 pounds (32 kilograms)—a gain of 2 pounds since her discharge in May (Table V). At this time there was but 0.1 per cent. of sugar in the urine, but the blood-sugar was 0.27 per cent., the reaction for diacetic acid in the urine showed only a trace, and the CO_2 tension of the alveolar air was 31 mm. Hg. During the first day in the hospital she received 5 per cent. vegetables 300 grams, equivalent to 10 grams of carbohydrate and 5 grams protein, but no other protein and no fat, and with this the diacetic acid disappeared, not to return during her stay, which ended January 8, 1917. Upon the above diet the sugar promptly fell to a trace and disappeared entirely the following day. The diet was gradually increased, but the patient did not tolerate more than 15 grams of carbohydrate, 32 grams of protein, and 23 grams of fat, amounting to 14 calories per kilogram of body weight. Even upon this meager ration I am sorry to add that the blood sugar, which had fallen in the early days of treatment to 0.16 per cent., rose to 0.24 per cent. when she left, at which time she was taking 10 grams of carbo-

hydrate, 33 grams of protein, and 35 grams of fat, the equivalent of 17 calories for each kilogram of her body weight. Note the contrast with the diet at her discharge from the hospital on her first visit, when the calories were 50 per kilo body weight.

The third entrance of this patient to the hospital was on September 13, 1917. (See Tables IV and V.) Her condition was then far more precarious. The weight was 58 pounds (26 kilograms), blood-sugar 0.36 per cent., Wishart acetone test quadruple positive (++++), and in the urine the sugar amounted to 3.3 per cent., the reaction for diacetic acid was triple positive (+++), the ammonia 2.5 grams in twenty-four hours, the CO_2 tension of the alveolar air in terms of mm. Hg. pressure was 14, the lowest reading with discharge of the patient from the hospital alive in my personal experience, though Dr. Geyelin has shown recovery, also without alkalis, to be possible even under more adverse conditions. Two days later the CO_2 in the blood was equivalent to 21.3 mm. Hg. The breathing at entrance was distinctly labored—the hyperpnea characteristic of diabetic coma. Fortified by the experience with this patient at the time of her first entrance when she also showed acidosis, as well as by results with other patients, I adopted the same plan of treatment as before, namely, the omission of fat and the feeding of a small quantity of carbohydrate followed by fasting. The details are shown in Chart IV. This time, however, the acidosis was more severe, and despite three days of feeding and two days of fasting, both acidosis and sugar remained present in the urine. The patient, therefore, was fed for the three subsequent days on 5 grams of carbohydrate and 27 grams of protein—the approximate amount contained in 150 grams of 5 per cent. vegetables and 120 grams of fish; but even on the third day of this limited diet the sugar amounted to 22 grams in the urine and the diacetic acid was still present. Indeed, it required a day of fasting, a similar day of restricted diet, followed by four alternate days of feeding and fasting, and then three days of complete fasting, save for 15 grams alcohol, until the acid disappeared and the sugar was reduced to a trace. With this general plan of treatment the urine became entirely free from sugar on

TABLE V

CASE NO. 1012

No. of visit.	Date.	Length of stay (weeks).	Condition at entrance.					Condition at discharge.				
			Urine.		Blood-sugar, per cent.	Alveolar air, CO_2 mm. Hg.	Wt., kilos.	Urine.		Blood-sugar, per cent.	Alveolar air, CO_2 mm. Hg.	Wt., kilos.
			Diacetic acid.	Sugar, per cent.				Diacetic acid.	Sugar, per cent.			
First	March 13, 1916	10	++++	4.4	0.36	34	31	0	0	0.13	34[1]	31
Second	Dec. 22, 1916	2½	+	0.1	0.27	31	30	0	0	0.24		29
Third	Sept. 13, 1917		+++	3.3	0.36	14	27	0	trace	0.29	37	26

[1] Two weeks before discharge.

October 11th—twenty-nine days after entrance. However, these persistent efforts were rewarded, because from November 8, 1917, until the discharge of the patient, December 31, 1917, sugar occurred only on two days, and then was only a trace, the diacetic acid was invariably absent, and the CO_2 tension in the alveolar air was 37 on discharge. In other words, she is a severe case of diabetes, but without acidosis. The blood-sugar, which had remained persistently high, gradually fell to 0.18 per cent. on December 20, 1917. The diet upon which the patient now lives consists of 3 grams of carbohydrate, 55 grams of protein, 40 grams of fat, and 5 grams of alcohol, making 627 calories, amounting to 24 calories per kilogram body weight. The patient will be discharged with this régime and instructed to stay upon it, with a fasting day each week. She is not to increase it unless the blood-sugar falls to normal. Should sugar appear, fasting is to be followed for a day, and for the subsequent two weeks thrice washed vegetables are to replace the 3 grams of carbohydrate which she now receives.

Other features of this case to which I would call your attention are the gradual return of the alveolar air to a normal figure of 36 on November 6th, and 37 on December 31st. For three weeks the alveolar air remained in the neighborhood of 32 and 33. In a debiliated individual, however, it is not uncommon to find the alveolar air somewhat reduced.

TABLE VI

THE OMINOUS INCREASE OF THE BLOOD-FAT OF CASE NO. 1012 DESPITE HOSPITAL TREATMENT

Date. 1917	Blood-fat (per cent.) (Bloor).
November 7	0.69
November 20	0.88
December 5	1.03
December 13	1.25
December 20	0.998
" 27	0.817
" 30	0.895

The *blood-fat* (Bloor's fat) on October 15th was 0.823, in contrast to 0.60, which would be a normal value. On November

7th it was 0.69. On November 20th, when the patient's diet had been only increased in a limited way, the blood-fat had risen to 0.88. On December 5th an increase up to 1.03 was noted, and by December 13th this had risen again to 1.25—unwelcome evidence, I must confess, of a pathologic condition which at present is difficult to combat. Subsequent values were lower. (See Table VI.)

Always court graphic demonstration of failures quite as much as of successes in treatment. The unvarnished truth is always helpful. By thus calling your attention to these figures I fully expect that some one of you in years to come will help to improve upon them. I wish that one could say of the blood-fat as it is possible to say of the blood-sugar in an elderly diabetic, that such an increase is borne apparently without harm to the individual, but I cannot even take this comfort, and must acknowledge that this is the most ominous sign which now confronts this patient. However, we are in the early days of our knowledge of blood-fat, and we must not be discouraged. It is a great gain to have discovered the enemy, and we can find some solace in the thought that this patient is traveling in a region into which none under our care have hitherto penetrated.

How recent is our knowledge of the blood lipoids my own data illustrate. It is only two years ago that there existed but 28 complete blood-fat analyses which had been made upon all of my patients, and these were completed that year entirely through the kindness of Professor Bloor. Last year 131 similar analyses were performed by my assistant, now Lieutenant Horace Gray, also working in Professor Bloor's laboratory, but already within the first four months of this winter's work Miss Warren, in the laboratory of the New England Deaconess Hospital, has completed 116 determinations, though in this latter series only the fat by Bloor's method was sought, since this method appeared the best for clinical work. With the accumulation of these analyses, the ground is being broken for future therapeutic advances. In this connection may I emphasize the importance of the aid which the increased accuracy of chemical methods has brought to the treatment of diabetes? It is perhaps best shown

in the tests relating to acidosis, though valuable information has also come from a more intimate knowledge of the blood-sugar. In 1901 I journeyed all the way to Strasburg to learn from Professors Naunyn and Magnus-Levy, then Privat-docent, the most recent methods for measuring the acidosis of my patients. At that time the Schlossing test for ammonia was the most available, but that test required, after the collection of the twenty-four-hour urine, three days for its completion. Subsequently, Folin shortened the method to less than half an hour, but even then the test was performed at the end of a twenty-four-hour urinary collection, and though one might draw conclusions as to the quantity of ammonia by estimating the amount voided in shorter periods, the plan was seldom adopted. Contrast our armamentarium of today, when in ten minutes we can determine the degree of acidosis of our patient by the decrease in the carbon dioxid content of the alveolar air. And the method is so simple that I make a point of having all my diabetic nurses trained to perform it. I am glad of the opportunity of having it demonstrated here by Miss MacDougall, for I wish to impress upon you that it is with women that your competition will lie in the immediate future. In fact, all my chemical work now is performed by Miss Warren, Miss Amory, Miss MacDougall, and my secretaries, Miss Leonard and Miss Wood—such changes has the war wrought!

Both the Fridericia and the Marriott tests for the carbon dioxid content of the alveolar air are admirable, but the latter is more compact and has the advantage that it can be more easily applied to a child or an unconscious patient. The values obtained from it are a trifle higher than those obtained with the Fridericia apparatus.

Contrast the confidence with which a physician begins the treatment of a case of acid poisoning today with that of fifteen years ago. Today, by the Folin, or by another, the simple Malfatti test, one can quantitate the urinary ammonia within a few minutes, or, if preferred, by the determination of the carbon dioxid in the alveolar air can obtain a knowledge of the intensity of the acid poisoning on the spot. Forewarned is to be forearmed.

Since all cases of diabetic coma pass through a stage of acidosis as severe as the stage from which our little case was rescued, it is obvious that treatment of milder cases along similar lines ought to remove them from danger. This possibility I believe to have been attained. The statistics already cited furnish the proof for this statement.

Summary of Deaths from Diabetes at the Corey Hill and New England Deaconess Hospitals During 1917.—My own statistics for this last year show 181 cases treated at the Corey Hill and New England Deaconess Hospitals, with 4 deaths, or a 2 per cent. hospital mortality. These 4 cases are typical of many others, but they are so fresh in my mind that I will briefly summarize them. I am glad to do this, because it is from mistakes that one learns, and, furthermore, it is always wise for doctors who are constantly working with variables and uncertainties to come face to face with facts—and deaths are facts.

Case No. 1431, a little child who developed diabetes at the age of four years and four months in October, 1917, was put on the train 500 miles from Boston while showing the deep breathing of diabetic coma. This steadily increased until I saw her the next day for the first time at the hospital. She was conscious, had eaten eggs and bacon a few hours before, but was restless, and hyperpnea was evident to all. The regulation rules for the treatment of threatening coma which are in force at the hospital were adopted, but these proved to be of no avail, and the little child succumbed the following day. This is another one of the cases which has made me term *the first year following the detection of the disease the diabetics' danger zone. Had this child undergone "preparatory treatment," already described to you* (see page 903), *I believe the complication of acidosis thus early in the disease would not have arisen.*

The rules which have proved useful are given below. My experience with this child has made me add an eighth, now numbered "4," relating to gastric lavage. It is possible that if I had acted in accordance with it this patient might have been at least temporarily saved.

THE TREATMENT OF THREATENING DIABETIC COMA

Rules in Force at the Corey Hill and New England Deaconess Hospitals

1. *Nursing.*—Provide a special nurse for the patient both day and night, preferably, one trained in diabetic work.

2. *Bed.*—Keep the patient in bed and warm. Avoid loss of calories through exertion or exposure; if restless, protect from becoming chilled by flannel night-clothes. Every effort should be made to allay nervousness and discomfort.

3. *The Bowels.*—Move the bowels by one or more enemata. Cathartics should usually be avoided for fear of causing diarrhea.

4. *The Stomach.*—This should be free from indigestible food. With adults, when in doubt, but with children in all cases, begin treatment with gastric lavage.

5. *The Heart.*—Sustain the circulation with the help of digitalis. Caffein may be given subcutaneously, or as black coffee by rectum.

6. *Administration of Liquids.*—Give 1000 c.c. of liquids within each six hours. The liquids are to be given slowly, hot, as coffee, tea, thin broths, water; if the prospect is dubious of giving so much liquid by mouth, salt solution or tap-water is to be given by rectum; if this resource fails, the nurse should call the doctor to give intravenously the balance of the liter which remains not given for the period. (It will seldom be found necessary to give more than 1000 c.c. liquids, thanks to the avoidance of alkalis.) In order to secure the introduction of sufficient liquid in the first six hours the cleansing enema at the beginning of treatment should be followed after half an hour by an enema of 500 c.c. salt solution in all cases as a matter of precaution.

7. *Diet.*—If the patient has been accustomed to the fasting method of treatment, begin or continue the fast, but if he has been upon a full diet, give 1 gram of carbohydrate per kilogram body weight during the twenty-four hours in the form of orange-juice or gruel (oatmeal) made with water; whichever course is adopted, it is to be followed until danger is over.

8. *Alkalis.*—Avoid alkalis. If such have been previously given, omit at the rate of 30 grams a day.

Two of the deaths occurred in men—Cases Nos. 1381 and 1412. They so closely resemble one another that they can be described together. Each came to the hospital presenting, it is true, only moderate signs of acidosis, but excreting really enormous quantities of sugar in the urine—probably 1½ and possibly 2 pounds during the twenty-four hours immediately prior to entrance. The precaution was taken to omit fat at once and to prescribe a diet which contained about 200 grams of carbohydrate. In the one case, unfortunately, indigestion resulted from the vegetables employed, vomiting ensued, and was not stopped until acidosis had become so severe that it was not amenable to present-day treatment. This was all the more regrettable because it was a death during the first year of the disease. In the other patient even the restriction of the carbohydrate to 200 grams constituted so violent a change from the preceding diet that acidosis increased and death resulted. From the friends of this patient I learned that his disease was of three and three-quarters years' duration, and from himself that he had deliberately broken all bounds of diet for several months prior to admission to the hospital, claiming in justification, and with some show of reason, that he had eaten carbohydrate freely so as to avoid acidosis. *To cases like these in the future I shall be inclined to give as much carbohydrate in the diet as they excrete in the urine for each successive preceding twenty-four hours, and only then gradually lower the carbohydrate. This is exactly what I have urged in the preparatory treatment for fasting, but hitherto I have depended upon the statements of the patient as to the amount of carbohydrate in the diet; henceforth I believe it will be safer to be guided by the sugar actually excreted in the urine for the preceding twenty-four hours, twelve hours, six hours, or even less.* Such measures I hope will save many of these cases.

I am more skeptical about saving individuals like Case No. 1070, the fourth patient who died. She entered the hospital showing the deep respiration of beginning coma, with carbon dioxid content of the alveolar air equivalent to 11 mm. Hg. tension, remained under my care for twelve days, and then succumbed. In the interim the alveolar air rose to 16 mm. Hg.

This patient had been in the hospital sixteen months previously during the fifth month of her pregnancy, and at that time showed severe acidosis which was successfully treated by my assistant, now Lieutenant A. A. Hornor. She returned for a cesarean section, which was performed under local anesthesia by Dr. J. C. Hubbard, and during the succeeding year lived happily and brought up a healthy child.

Presentation of the Second Case.—The second patient, Case No. 1011, whom I am to show you, is slight and thin like our first case. She first noted polyuria and loss of weight in May, 1914, at the age of twenty-four years and ten months, but the disease was not diagnosed until five months later. A history of obesity or heredity was absent, but preceding the onset of symptoms was an attack of influenza of a few days' duration. Between October, 1914, and her first visit to me in March, 1916, glycosuria was absent for much of the time. Her weight was then 40 kilograms, in contrast to her highest weight recorded of 57 kilograms; the diacetic acid in the urine was +++, the sugar less than 1 per cent., and the alveolar air 25. The sugar fell to a trace upon fasting for two days, and following three days of feeding with 10 grams of carbohydrate, 21 grams protein, and 6 grams fat, and another fasting day, disappeared entirely, but acidosis persisted. It is interesting to contrast this case with the first case I brought before you, for from the diet of this patient fat was not totally excluded for a long period, and to this fact I attribute the persistence of acidosis for some six weeks. The patient was finally discharged after ten weeks, with the urine free from sugar and diacetic acid, and upon a diet of 5 grams carbohydrate, 63 grams protein, and 81 grams fat (Table VII).

She returned to the hospital in August, 1916, sugar and acid free, with the hope of increasing her tolerance for carbohydrate. This was accomplished so far as the urine was concerned, and she left on September 2d, taking 44 grams carbohydrate, 40 grams protein, and 63 grams fat, but I must acknowledge that the blood-sugar was 0.25 per cent. Her weight was then 31 kilograms.

Again in October, 1916, she returned for her third visit, this time with quite severe acidosis, which, however, promptly yielded

TABLE VII

THE CONDITION AT ENTRANCE AND DISCHARGE OF CASE NO. 1011 DURING REPEATED VISITS TO THE HOSPITAL

No. of visit.	Date.	Length of stay (weeks).	Condition at entrance.					Condition at discharge.				
			Urine.		Blood-sugar, per cent.	Alveolar air, CO_2 mm. Hg.	Wt., kilos.	Urine.		Blood-sugar, per cent.	Alveolar air, CO_2 mm. Hg.	Wt., kilos.
			Diacetic acid.	Sugar, per cent.				Diacetic acid.	Sugar, per cent.			
First	March 15, 1916	10	+++	0.6	0.28	25	40	0	0	0.24[1]	30	38
Second	Aug. 14, 1916	2½	0	0	0.27	34	33	0	trace	0.25		31
Third	Oct. 24, 1916	2½	++++	1.3	0.34	24	30	0	0	0.19	29[2]	29
Fourth	April 20, 1917	8	+++	1.6	0.28	22	28	0	0	0.12		31
Fifth	Sept. 25, 1917	12½	++++	4.5	0.33	15	26	0	0	0.08	34[3]	28

[1] Four weeks before discharge. [2] Five days before discharge. [3] Ten days before discharge.

to withdrawal of fat, and the sugar disappeared as well within nine days. At this time she left with a diet containing 6 grams carbohydrate, 42 grams protein, and 44 grams fat. The blood-sugar was 0.19 per cent., but the weight showed a steady fall to 29 kilograms.

A fourth visit to the hospital was made in April, 1917. This time acidosis was also severe and the sugar amounted to 22 grams over night. A prolonged fast of five days, save for a little alcohol, brought about the disappearance of acidosis, but sugar did not disappear until seven days later, during which period she was allowed a little protein and an insignificant amount of fat, a little alcohol, but no carbohydrate. She was discharged on June 15, 1917, this time with her lowest blood-sugar so far, namely, 0.12 per cent. Her diet was made up of carbohydrate 9 grams, protein 53 grams, and fat 61 grams, with 12 grams of alcohol. The weight was 31 kilograms.

However, the patient experienced much difficulty in keeping sugar free at home, and finally broke over the diet, returning to the hospital for a fifth time in September, 1917, with diacetic acid ++++, 4.5 per cent. of sugar, blood-sugar 0.33 per cent., and alveolar air 15 mm. Hg. Upon this occasion the diet prescribed was as nearly as possible that preceding entrance, but minus fat. This established the carbohydrate at approximately 100 grams and the protein at 67 grams. *The acidosis, which was not overcome for weeks on a former occasion, disappeared this time in three days (!)—a tribute, I take it, to the complete elimination of fat and the non-reduction of carbohydrate* (Table VIII).

Tests with High Carbohydrate Feeding and Variations in the Protein and Fat.—The patient had been through the fasting treatment so many times that both her parents and she now desired that a different method of treatment be adopted. This I felt proper, and I arranged a series of diets to be followed for periods of about ten days each, by the first of which the acidosis might be completely eradicated, and in subsequent periods the effect of protein and fat noted. I hoped by the complete elimination of the acidosis to lessen the severity of the diabetes as well. In a way, this was accomplished, for at the conclusion of the

TABLE VIII

SUMMARY OF FIFTH VISIT TO THE HOSPITAL OF CASE NO. 1011

Date, 1917.	Urine.				Diet, grams.					Balance.		Blood.		Alveolar air, CO_2 mm. Hg.
	Volume, c.c.	Reaction.	Diacetic acid.	Sugar, gms.	Carbohydrate.	Protein.	Fat.	Alcohol.	Calories.	Carbohydrate.	Carb.-protein.	Sugar, per cent.	Fat, per cent. (Blood).	
Sept. 25	specimen 20°		++++	4.5%								0.33		15
25–26	4400		+++	145										16
26–27	3200		+++	162	117	70	0	15	853	−45	−3			18
27–28	2100		++	101	99	67	0	15	769	−2	+38			19
28–8 Oct.	2602	acid	0	82	99	67	0	15	769	+17	+57	0.29		27
8–12	2950	acid	0	67	99	31	0	15	625	+32	+51	0.31	1.76	
12–13	3200	acid	0	83	99	36	28	15	897	+16	+48		1.326	34
13–24	3474	acid	0	78	99	36	40	15	1005	+21	+43	0.30	1.326	32
24– 3 Nov.	3538		0	99	129	29	40	15	1097	+30	+47	0.33	0.997	
3–14	3077	sl.	0	88	105	82	40	15	1213	+17	+66	0.29	1.094	31
14–22 Dec.	2967	acid	0	51	81	51	21	15	822	+30	+61	0.24	1.007	34
9–10	3400	neut.	0	0	0	0	0	23	161	0	0		1.161[1]	
10–13	2700		0	0	0	40	16	15	409	0	+24	0.12	1.206	34
13–14	2700		0	0	0	43	24	8	444	0	+26			
14–16	3250		0	0	0	45	31	8	515	0	+27			
16–17	2650	neut.	0	0	0	53	36	8	592	0	+32	0.08		
17–18	3700	sl.	0	0	0	0	0	23	161	0	0			
18–22	2413	acid	0	0	1	53	36	8	696	+1	+32			

periods the existing glycosuria of 50 or more grams disappeared with a day and a half of fasting, in contrast to the prolonged periods required to accomplish this end at her former visit.

In Table VIII you will note that acidosis disappeared within three days when fat was removed from the diet, and the patient given a quantity of carbohydrate not far from what she had been taking outside. For example, in the first twenty-four-hour period, September 26–27, 117 grams were given, but there appeared in the urine 162 grams, giving a minus carbohydrate balance of 45 grams. On the following day, when the carbohydrate was changed to 99 grams, this minus balance dropped to minus 2 grams, and during the subsequent ten days, when the diet was essentially the same, changed to a positive average daily carbohydrate balance of 17 grams. If we look at the matter in

[1] December 4th.

another way and add to the 17 grams the carbohydrate which could be formed out of the 67 grams protein allowed, on the basis that for each 100 grams protein 60 grams carbohydrate are produced, the carbohydrate balance would be still higher, and would be as follows: Carbohydrate 99 grams + carbohydrate formed from protein (67 grams × 60), 40 grams = 139 grams, minus the 82 grams sugar excreted daily in the urine = 57 grams —that is, a daily positive combined carbohydrate balance of 57 grams.

During the period October 8–12 the protein was reduced to 31 grams, and although the carbohydrate balance rose to 32, the carbohydrate balance of the carbohydrate and protein together fell. Between October 13th and 24th, without essential change in the protein, nearly 400 extra calories in the form of fat were added to the diet. The carbohydrate balance was essentially the same as that on the carbohydrate and low protein diet, and the carbohydrate balance based on combined carbohydrate and protein intake improved. Between October 24th and November 3d 30 grams additional carbohydrate were given, leaving the protein and fat essentially the same. However, this was disadvantageous, for two-thirds of it appeared in the urine. The carbohydrate was then put back to 105 grams between November 3d and 14th, and the protein raised to approximately 3 grams per kilo of body weight, and the fat unchanged. As a result the carbohydrate balance dropped, but the carbohydrate-protein balance reached its highest figure. The final change in the diet was made, preliminary to getting the patient sugar free by fasting, by lowering the carbohydrate to 80 grams, and giving 1.5 grams protein and about 1 gram fat per kilo of body weight. On this diet both the carbohydrate balance and the carbohydrate-protein balance remained high, and this seemed to be the best arrangement of all. Following fasting the patient finally attained a diet containing 1 gram carbohydrate, 53 grams protein, 36 grams fat, and 8 grams alcohol, making 696 calories, without showing sugar in the urine, and having remained sugar free upon it for some days, she was allowed to go home.

During these various tests you will see that experiments were made with carbohydrate, with large and small quantities of protein, with fat absent, and with fat present in moderate amounts. Throughout all these changes acidosis remained absent, and while upon a diet of 80 or more grams carbohydrate a positive carbohydrate balance was maintained. The food-supply appeared ample because the large quantity of carbohydrate allowed so much bulk. Yet—and to this I call your especial attention—if one estimated the net calories retained by the patient by deducting the amount of calories lost as sugar in the urine, you will see that the diet was still an undernutrition diet. Subsequent to the brief fast the patient was able to take a few grams of carbohydrate, and though the caloric intake was lower than before, the net calories approximated the same as when the high carbohydrate diet was allowed.

At the conclusion of these observations independently both the patient and I agreed that the high feeding, although more agreeable than fasting, had been distinctly harmful so far as the diabetes was concerned, but upon the acidosis the effect had been favorable. No case has been treated similarly by me, and I have followed no case and know of none accurately followed under precisely these conditons. The tests which this patient was glad to have made, however, prove one point, that the elimination of fat and the allowance of carbohydrate do cause an essential change in the metabolism of a diabetic, and to be conservative, allow us to say at least this—that whereas such a patient with restricted dieting became sugar free only after periods of many days, upon a diet with restricted fat but high carbohydrate it was possible with a subsequent fast to become sugar free in a few days.

Efforts to Reduce the Blood-sugar to Normal.—If you will glance at Tables IV, V, VII, and VIII you cannot fail to be impressed with the high percentages of blood-sugar despite the fact that these patients have been under my care for several years. Occasionally the values have fallen to nearly normal, but it must be confessed that treatment has not been satisfactory in this regard. In a conference with Dr. Allen, he was good enough

to point out that in some of his cases he had been able to secure a normal blood-sugar when the patients lived upon an undernutrition diet with food exclusively in the form of protein. By this means during the period of underfeeding the body strength was, to a considerable extent, sustained. Adopting his suggestion with both of these patients, you will see that I have had more success than hitherto, for the blood-sugar of Case No. 1011 in this way was brought to normal and the blood-sugar of Case No. 1012 fell perceptibly, unfortunately to rise on the morning of discharge, when the diet was carbohydrate 3 grams, protein 55, fat 40, and alcohol 5 grams.

There is little doubt that if the blood-sugar is normal there is less liability of the return of glycosuria. Repeatedly I have been mortified upon sending patients home after they have been sugar free in the hospital for several weeks to learn a few days later that sugar had returned, although no change had been made in the diet. Therefore, if one can secure a sugar-free urine, which has been hitherto our standard of treatment, by keeping the blood-sugar normal one will feel far more at ease.

It is still a question with me whether it will be advisable to take such heroic measures to keep the blood-sugar constantly normal. My reason for hesitation in this regard is that patients who have had diabetes for years, yet only occasionally developing glycosuria, often show an increased quantity of sugar in the blood and yet appear in excellent condition. Perhaps this is due to the impairment of their kidneys. To reduce the blood-sugar to normal in these patients would probably require extremely strenuous measures, and before I should adopt such a plan as a routine I should wish to try it out first in a moderate way. Fortunately, with the increasing ease with which blood-sugar determinations are being performed, there is little doubt but that new light will soon be shed upon this point.

Efforts to Reduce the Blood-fat.—The blood-fat is far less easily brought down to normal than the blood-sugar. Our first patient is an example in point. With Case No. 1415, for example, showing a blood-fat on October 20, 1917, of 2.8 per cent., although she has been on a low diet and one containing

very little fat, and although the blood-sugar has dropped from 0.31 to 0.10 per cent., the blood-fat still remains (December 12, 1917) at 2.17 per cent.[1] On her prolonged low diet, tolerance has risen, and she now enjoys 28 grams carbohydrate. I hope that gradually the blood fat will fall, for I can hardly believe that her diabetes is under control with a blood-fat three times the normal. It is certainly gratifying to see her walk about, because prior to her entrance to the Corey Hill Hospital she had not been able to dress herself or walk for ten months. Here again routine laboratory tests will give us data which will be of inestimable advantage. The simplification of the method for the estimation of blood-fat which Prof. Bloor has wrought must yield large results. All these improvements, however, really represent improvements in degree rather than radical advances in treatment, but I am so confident that our modern methods of treatment of diabetes are satisfactory for the overwhelming majority of cases that, although not content with the gains which are being made, I am at least encouraged by them.

Changes in Weight.—Case No. 1012. This case showed such remarkable changes in weight during the first twenty days in the hospital as to deserve your notice. The increase amounted to 25 per cent. One not experienced in the treatment of diabetes might at first conclude that a wonderful progress was being made by the patient. Physical examination, however, would quickly dispel this illusion, for edema was marked within eleven days of her entrance. Furthermore, the total quantity of food which the patient ingested for these twenty days furnishes proof that the gain in weight could not have been gain in body tissue, for the calories consumed, not allowing for those lost in the urine in the form of sugar, amounted to 5.5 calories per kilo per twenty-four hours, and if we reckon the net calories, this figure is reduced to 2.9 calories.

One should invariably take into account such collections of water in the body when arranging the diet. Obviously, this accumulated water should not be reckoned in the same way as body tissue so far as relates to body requirements for food. This

[1] One month later it had fallen to 1.5 per cent.

is often overlooked in our estimations of the needs of the patient, and, furthermore, overlooked in reckoning the metabolism of such patients from day to day. When one considers that the gain in weight amounted to 25 per cent., it is obvious that unless attention is paid to this possibility conclusions as to the total metabolism of an individual, if reckoned per kilo of body weight, would be far askew. This point strikes me as a very important one, and I do not remember to have ever seen it receive the attention it deserves.

The Total Metabolism.—The metabolism of patients with severe diabetes has interested Professor Benedict of the Nutrition Laboratory of the Carnegie Institution of Washington situated here in Boston and myself for many years. This patient, Case No. 1011, has frequently been a subject for study, and during her present stay at the hospital 16 tests of more than two hours' duration each have been made of her metabolism in the respiratory chamber in the Respiratory Laboratory fitted up by the Carnegie Institution at the New England Deaconess Hospital. One-half of these tests were made in the postabsorptive period—that is, at 8 o'clock in the morning, approximately fourteen hours after the last meal. The balance of the tests were made either after breakfast or after the noon meal. Many interesting data were observed, but in this place it is appropriate to discuss only the general features, and I do this with reserve, because as yet Professor Benedict and I have not discussed them in detail or submitted the data to final corrections.

The total metabolism was determined in each experiment, and as you are more familiar with the caloric requirements of the normal individual per kilo of body weight for twenty-four hours, I am giving the results in this form, though in reality it is more correct, in describing metabolism for a limited period, to report the results in calories per hour. The average heat production per kilo of body weight on a twenty-four-hour basis for the eight postabsorptive experiments was 28 calories per kilo per twenty-four hours. The latter two observations were 26 and 25 calories respectively, whereas the earlier six experiments showed a variation between 28 and 32 calories. The departure of any of the

figures, however, from the average above mentioned was not great, even with the wide variations of diet prescribed. The difference between the earlier and later figures is distinct, but not sufficiently striking to warrant me in drawing definite conclusions at the present time. In general, it may be said that the metabolism did not essentially differ from normal individuals of similar size and weight.

The metabolism following the ingestion of food showed wider variations, for the lowest observation showed an output of 29 calories per kilogram of body weight per twenty-four hours, and the highest 40, the average being 33. Here again the metabolism for the last two observations, like that of the last two postabsorptive experiments, tended to the lower limits, being 29 and 32 calories respectively. The striking increase in metabolism following a meal is a hopeful phenomenon, for it shows that this diabetic subject will still respond to food.

The respiratory quotient also furnishes proof that food was utilized. You will remember that the relation of the volume of carbon dioxid exhaled to the volume of oxygen absorbed in any given period constitutes the respiratory quotient. This will amount to 1.00 when carbohydrate ($C_6H_{12}O_6$) is burned, because enough oxygen is present in the molecule to combine with the hydrogen and all the oxygen required for oxidation may unite with the carbon. But with protein the respiratory quotient drops to 0.81, because extra oxygen is required for oxidation of the non-carbon atoms in the protein molecule, and this is still more the case with fat, for so much oxygen is demanded that the respiratory quotient drops to 0.71. The most interesting feature about this patient is the high respiratory quotient which she presented even after fasting. We think of a severe case of diabetes —and certainly this was such—as devoid of carbohydrate reserve supply and as unable to burn carbohydrate, and formerly the average respiratory quotient of such patients was found to be about 0.73, yet this patient was able to maintain a respiratory quotient consistent with the burning of large quantities of carbohydrate. The explanation of this phenomenon remains an enigma, and is one of the most interesting puzzles of the diabetic

problem today. The average of the eight observations on the respiratory quotient in the postabsorptive area was 0.82, while the average of the eight observations upon the respiratory quotient after the ingestion of food was 0.88—so great an increase and so far above the respiratory quotient for protein that one could not explain it as due to protein. The high postabsorptive respiratory quotient of the diabetic unable to ingest carbohydrate without the appearance of sugar in the urine, and therefore living upon protein and fat, is difficult to explain, and the explanation of this further rise in the respiratory quotient after food is certainly not easier.

These two patients whom I have shown you, as trustworthy as any who are likely to come under your supervision, illustrate the difficulties with which one must contend in diabetes. Each, in my estimation, has withstood the disease longer than other diabetic patients under my care of equal intensity. Each has pushed the boundary of life a little farther, and in so doing has helped to advance treatment. By living they have helped lower a hospital mortality which has averaged 27 per cent. yearly for ninety years to a hospital mortality of 2 per cent.—certainly no mean achievement. Their recovery from severe acidosis is unusual, and that it should have taken place without the use of alkalis is more than any of us would have thought possible three years ago. The persistence of the high blood-sugar, and yet the demonstration of its being lowered by undernutrition and a protein diet, as suggested by Dr. Allen, deserves consideration. The resistance of the blood-fat to treatment gives a distinct problem for future work. The harmfulness of high carbohydrate feeding upon the disease diabetes, but its usefulness when combined with the exclusion of fat from the diet in the overthrow of severe acidosis appears plain. The temporary gain in weight due to edema, amounting in one of the patients to 25 per cent., should be mentioned. The approximately normal metabolism, including a respiratory quotient also not far from normal both in the postabsorptive and after food periods, are facts which deserve the closest scrutiny and present problems which

only intelligent and prolonged experiments can solve. Whereas the two cases are evidence of real progress in the treatment of diabetes. I am sure you will agree with me that the need for new discoveries in the management of such patients is imperative.

CLINIC OF DR. JOHN LOVETT MORSE

CHILDREN'S HOSPITAL, BOSTON

EMPYEMA IN CHILDREN: DIFFERENTIAL DIAGNOSIS AND TREATMENT

November 30, 1917.

GENTLEMEN: The case which I am going to discuss with you today seems to me a very interesting and instructive one because it illustrates so well the importance of a thorough physical examination and the careful and intelligent analysis of symptoms and signs.

This little boy, who is four and a half years old, is the first child of healthy parents. There is no tuberculosis in either family, and he has had no known exposure to tuberculosis. He has always been subject to "colds," but has not had one since his tonsils were removed last February until the beginning of his present illness. His general condition has also been much better since that time.

He was taken suddenly sick with what was apparently a "cold," October 22d. His temperature rose to 103° F., and his pulse and respiration were rapid. He developed a slight cough the next day. The temperature, pulse, and respiration were all normal on the 24th. Physical examination showed nothing abnormal in the lungs. His temperature rose again to 104° F. October 25th. It continued between 103° and 104° F. and, according to his physician, signs of bronchopneumonia developed on the right side on October 28th. He complained considerably of pain in the right chest in front. About the first of November his temperature began to break in the morning, and since that time has ranged between normal in the morning and 102° and 103° F. in the afternoon. During this time

his pulse has been about 140 and his respiration 40. The doctor says that the signs have persisted in the right chest and that recently they have seemed to him more like those of lobar pneumonia than of bronchopneumonia. The cough has continued and he has at times perspired profusely and has had slight chills. He has lost a great deal of weight and has taken his food very poorly. He vomited rather frequently in the beginning, but during the past week has not vomited oftener than once a day. He had six or eight loose stools daily up to two weeks ago, since when he has had only one or two daily. The abdomen has been distended at times. He was brought to the hospital yesterday, November 29th.

The so-called "cold" which he had October 22d and 23d may have been either an acute infection of the nasopharynx, as was supposed, or the onset of the illness which began October 25th. On the chances, it is probable, because of the normal pulse and respiration on the 24th, that it was simply a "cold" and the forerunner of the real illness which began on the 25th. The diagnosis of bronchopneumonia on the right side which his physician made on the 28th seems hardly reasonable, because bronchopneumonia seldom comes on so acutely, does not ordinarily run a continuously high temperature, is almost never limited to one side, and is usually not accompanied by pain. Moreover, localized pain in respiratory affections usually points to an inflammation of the pleura on the affected side, and acute pleurisy is uncommon in bronchopneumonia. The story is far more consistent with the diagnosis of lobar pneumonia, for which the sudden onset, the continued high fever, the limitation of the process to one side, and the localized pain are most characteristic. The continuence of the high temperature without remissions until November 1st, seven days after the onset, when it began to break, is also very characteristic of lobar pneumonia. The irregular temperature during the last four weeks is consistent with bronchopneumonia, but it is not reasonable to suppose that the lesions of bronchopneumonia would remain localized in one lung all this time. Neither is it reasonable to believe with the physician that lobar pneumonia has taken the place of bron-

chopneumonia, especially when we take the irregular temperature into consideration. It is far more reasonable to believe that the physician is weak in physical examination and, therefore, to pay little attention to his findings and conclusions.

It is safe to conclude, then, that the boy had an attack of lobar pneumonia on the right side between October 25th and November 1st, and that the irregular temperature is due to some sequela of this attack. The chills and sweating suggest very strongly that there is a collection of pus somewhere in his body. They make it very improbable that the persistence of the signs in the lungs is due simply to an unresolved pneumonia. The facts that he has probably had lobar pneumonia, that abnormal physical signs have persisted on the right side, and that the rate of respiration has continued to be increased out of proportion to that of the pulse point very strongly to the right chest as the seat of this collection. If it is in the right chest, it may be either in the lung or in the pleural cavity. It is far more likely to be in the pleural cavity than in the lung, because purulent pleurisy is far more common than abscess of the lung. It is possible, however, that the pus may be located somewhere else, most likely in the middle ear or in the pelves of the kidneys, although the absence of all symptoms pointing to the ear makes it improbable that it is located there. Another possibility is that the trouble in the lung is tubercular. If so, it may have been tubercular from the first, or a primary pneumonia may have lighted up a pre-existing tubercular process. The absence of a tubercular family history and of known exposure to tuberculosis does not, of course, count in any way against this possibility, as at least 25 per cent. of all children of this age are infected with tuberculosis. The present symptoms are all consistent with this diagnosis. The chances are very much against it, however, as empyema is far more common after lobar pneumonia at this age than either an acute tubercular pneumonia or a secondary tubercular infection of the lungs. The loss of weight, the anorexia, the vomiting, the diarrhea, and the abdominal distention are all secondary symptoms and consistent with any of the possibilities. We approach the physical exam-

ination, therefore, expecting to find an empyema on the right side.

He has, as you see, evidently lost a great deal of weight. He is moderately pale. He is evidently perfectly clear mentally. His tongue is considerably coated. His throat shows nothing abnormal. His ear-drums are normal. The cardiac impulse is palpable in the fourth space, 7 cm. to the left of the median line. The left border of dulness corresponds to the impulse. It is impossible to locate the right border of the heart because of the flatness in the right chest. The action is regular and the sounds normal. The sounds are as loud to the right as to the left of the sternum. The second pulmonic sound is considerably accentuated. The right chest moves less than the left. There is no bulging of the intercostal spaces, and there is no apparent difference in the size of the two sides. There is tympany in the right front above the second rib. There is flatness below this and in the axilla and over the whole right back. The respiration is nearly normal in the tympanitic area. It is loud and bronchial over the flat area in front, diminished and bronchovesicular in the axilla and back. It is impossible to make out anything as to the voice sounds and tactile fremitus, because he will not talk and whines instead of crying. There is a very marked sense of resistance all over the flat area. Grocco's sign is absent. There are no râles. The left chest shows nothing abnormal, except that it is slightly hyperresonant and the respiratory sound is exaggerated. The abdomen is a little full, but otherwise normal. The liver is palpable 3 cm. below the costal border in the nipple line. The spleen is not palpable. The genitals are normal. The extremities show nothing abnormal. There is no spasm or paralysis. The knee-jerks are equal and normal. There is no Kernig's sign. There is no enlargement of the peripheral lymph-nodes. His rectal temperature is 102° F., his pulse 140, and his respiration 40.

The urine is high in color, acid in reaction, of a specific gravity of 1026, and contains no albumin or sugar.

The leukocyte count is 24,000.

The sputum has not been examined.

The tuberculin test was not done until this morning, too late to be of any assistance to us.

The physical examination shows conclusively that the seat of the trouble is in the right chest. The normal condition of the ear-drums shows that he has not got otitis media. The examination of the urine shows nothing more than concentration and excludes pyelitis. The accentuation of the second pulmonic sound means simply that there is increased resistance in the pulmonary circulation as the result of the lesion in the right lung and tells us nothing as to the nature of this lesion. The hyperresonance and the exaggerated respiratory sound on the left signify a compensatory enlargement of the left lung.

In view of the possibilities in this instance the first thing for us to determine is whether there is solidification of the right lung or fluid in the pleural cavity. After this has been decided, we will try to find out in other ways what is the cause of the solidification of the lung, if this is present, or what is the character of the fluid, if there is fluid. If there is an abscess of the lung the signs will be those of solidification of the lung, modified to some extent, rather than those of fluid in the pleural cavity. The fact that the right side does not move as much as the left in respiration does not help us any in this diagnosis, as it shows only that there is trouble in the right side, not what this trouble is. The absence of apparent enlargement of the right chest and of bulging of the intercostal spaces does not rule out the presence of fluid, but merely shows that there is probably not a large amount. The location of the cardiac impulse, 7 cm. to the left of the median line, and the fact that the heart sounds are as loud to the right as to the left of the sternum, show that the heart is in normal position. This point counts strongly against an effusion, but does not positively rule it out, because the heart may have been bound down by adhesions before the effusion formed. The absence of Grocco's sign is another point against effusion. It shows that the mediastinum is not displaced, but does not exclude an effusion, because the mediastinum is not displaced unless there is a considerable amount of fluid, and displacement may be prevented by adhesions. The fact that the liver is pal-

pable 3 cm. below the costal border in the nipple line at first suggests that it is displaced downward by fluid in the pleural cavity. As a matter of fact, however, the liver is not displaced downward by effusions in the right pleural cavity unless they are enormous, and seldom then. In this instance we already know from the absence of enlargement of the right side and bulging of the intercostal spaces that this is not the case. The abnormal position of the lower border of the liver must be due, therefore, to enlargement of the liver rather than to displacement downward. This enlargement is undoubtedly the result of the long-continued fever and the toxemia, and is, in all probability, due to fatty change, as it is too early for amyloid change to have taken place, even if there is pus in the pleural cavity.

The flatness in the right chest is consistent with either solidification of the lung or a pleural effusion. The tympany above the second rib is also consistent with either condition, being due presumably to loss of tension in the lung tissue. In the case of fluid this loss of tenison would be due to compression; in that of solidification of the lung, to compensatory emphysema. The normal character of the respiration at the apex is easy to explain if the lung there is simply emphysematous. If it is compressed by fluid, the sound should be bronchial. It is possible, however, that the normal vesicular sound is transmitted from the other side. The loud bronchial respiration in front is characteristic of solid lung. It is not inconsistent with a pleural effusion, however, because in children it is not at all uncommon to have loud bronchial respiration when the chest is full of fluid, probably because of the elasticity of the chest. It is difficult to explain the diminished bronchovesicular respiration in the axilla and back on the basis of solidification of the lung. If there is thickening of the pleura over a solid lung, the respiration might be diminished, but it should be bronchial. If there is no thickening of the pleura, the respiration should be loud and bronchial. It is also hard to explain the bronchovesicular character of the respiration if there is fluid in the pleura. This would, of course, explain the diminution in the intensity of the respiration, but the respiratory sound, coming from a compressed lung, should

be bronchial, not bronchovesicular. It is possible, however, that the bronchial sound from the compressed lung may be modified by the vesicular sound transmitted from the left lung. We shall have to get along without the assistance of the voice sounds and tactile fremitus, because he will not talk and whines instead of crying. The absence of râles is somewhat against solidification of the lung and in favor of an effusion into the pleural cavity, because, after five weeks, no matter what the cause of the solidification, there would probably be some breaking down of tissue or irritation of the bronchi, which would give râles. The very marked sense of resistance over the whole flat area is of great importance in diagnosis. By the sense of resistance I do not mean the sensation imparted to the pleximeter finger during ordinary percussion, but the feeling of resistance which is met when the chest is struck with the whole of the extended fingers, not with their tips. When the chest is struck in this way and the lungs are normal, there is a feeling of elastic resistance. When the lung is solidified, the feeling of elasticity is lost and the resistance is more definite. When there is any considerable amount of fluid in the pleural cavity the feeling of resistance is increased and becomes very marked. The sense of resistance is the same as that which is felt when the thigh is struck in the same way. It is the same whether the effusion is serous or purulent. Next to the presence or absence of displacement of organs it is to me the most important single sign in the diagnosis between solidification of the lung and pleural effusion.

Let us now sum up the results of our physical examintion of the chest and see if we can make up our minds from them whether there is solidification of the right lung or an effusion into the right pleural cavity. The findings obtained by percussion and auscultation of the right side are unimportant and must be disregarded, because they can be interpreted as consistent or inconsistent with either condition. The absence of enlargement of the right side and of bulging of the intercostal spaces is slightly against fluid. The absence of râles is slightly in favor of fluid. The normal position of the heart and the absence of

Grocco's sign are decidedly against fluid, while the very marked sense of resistance is very strongly in favor of fluid. The diagnosis thus depends almost entirely on the relative importance which we attach to the absence of displacement of organs on the one hand, and the marked sense of resistance on the other hand. It is easier to believe that the displacement of organs has been prevented by the formation of adhesions before the effusion became large enough to displace them than that the very marked sense of resistance is due to solidification of the lung. I feel very confident, therefore, that there is an effusion in the right chest.

Let us see now whether the laboratory findings are of any assistance to us either in confirming or disproving our diagnosis made on the history and physical examination. The white count of 24,000 is consistent with any and all of the conditions considered except a serous pleurisy, which almost always has a low white count. Even if the condition was tuberculosis of the lung, there would almost certainly be a mixed infection by this time and, therefore, a leukocytosis. The white count does not help us any, then, except in that it makes a serous effusion improbable. An examination of the sputum would not help us any unless tubercle bacilli were found in it. If they were found, we would know that he had tuberculosis of the lung, but we should not know whether he had also an effusion or not. If they were not found, we would be no better off than we are now. A negative tuberculin test would be strong evidence against the trouble in the chest being tubercular, but would not exclude it, because he is so ill that he might not react, even if it was tubercular. A positive test would, moreover, be of little importance, because at least 25 per cent. of all children of this age have been infected with tuberculosis. We get little or no help, therefore, from the laboratory findings. A Roentgen-ray picture would also be of little or no assistance in this case, because all of the conditions under consideration would give a dense shadow.

Having come to the conclusion that there is an effusion in the right pleural cavity, it is our duty to explore the chest to

verify the diagnosis because, if there is a serous effusion the fluid should be drawn off, and if it is purulent he should be operated upon at once. From the evidence which we have what sort of fluid ought we to expect to get? It will almost certainly be purulent if our reasoning has been correct. It is, we believe, secondary to lobar pneumonia, and in children such effusions are almost invariably purulent. The white count is strongly in favor of pus, and the irregular temperature, chills, and sweating are more characteristic of a purulent than of a serous effusion.

In general it is wise to introduce the needle in the place where the signs of fluid are most marked. In this instance it will probably make very little difference where we put it in, because he either has a chest full of pus or there is none in it. One of the best places to put in a needle, however, is in the scapular line in the seventh or eighth space, because it is an easy place to get at, the intercostal spaces are wide in this region, and there will surely be fluid there, if anywhere. We will, therefore, stick it in there. We will use a large needle, because, if the pus is thick, it will sometimes not run through a small needle. We will not use any local anesthetic, because that will hurt him and frighten him as much as the prick of the needle. The house-officer will hold him firmly, sitting up in his lap, with his left side toward him and his right arm stretched up in order to widen the intercostal spaces. We will now wash up the lower right back with soap and water and alcohol. Up to this time you will notice that nothing has been done to suggest to him that anything more than an examination is to be done. I am now going to tell him that I am going to prick him hard with a needle and that it will hurt him some, but only for a minute. He will find that this is true, and when I tell him in the future that I am not going to hurt him he will also believe that. Remember, never tell a child that you are not going to hurt him when you know that you are. If you do, he will never trust you afterward. If you always tell him the truth, he will always have confidence in you and you can do anything with him. If you deceive him, he will regard you in the same light as you yourselves do other liars. As I am simply going to explore his

chest, I shall use a needle attached directly to a syringe instead of an aspirator. This makes the operation much more simple, shortens the time, and diminishes the shock and fright.

The syringe is, as you see, full of thick, greenish-yellow pus, which confirms our diagnosis of empyema.

There is no question as to what ought to be done now. He should have a rib resected at once and the chest thoroughly drained. It is true that once in a great while an empyema can be cured by repeated tappings. This happens so seldom, however, that it is not only idle, but almost criminal to consider it. Simple incision between the ribs does not afford the free drainage that is possible when a rib is resected, and free drainage is necessary for a cure. The resection of a rib is a simple operation which takes but a little time, so that the shock of this operation is but little greater than that when a simple incision is done. If the resection is properly done, new bone will fill in the gap in the rib. A resection of a rib should always be done, therefore, rather than a simple incision, except in the very rare instances in which the child is too feeble to withstand the slight additional shock of the resection. In such instances a rib should be resected later. This boy is in relatively good condition and perfectly well able to stand a resection. We will therefore transfer him to the surgical side for immediate resection of a rib.

He will probably recover, because his digestion is now fairly good and his kidneys and heart show no evidences of infection. I fear, however, that it will be a good many weeks before the inflammation in the pleura will subside and the wound heal. I fear this, because I feel quite sure that, on account of the long duration of the inflammatory process in the pleura, adhesions have formed which are binding down the compressed lung. The normal position of the heart and the absence of Grocco's sign, taken in connection with the evidences of the large amount of fluid in the pleural cavity, confirm me in this belief. These adhesions will interfere with the rapid expansion of the lung and will delay the healing of the pleura. It is possible that they will prevent a complete expansion of the lung and that he will eventually recover with a permanent deformity of the right chest and more or less scoliosis.

CLINIC OF DR. W. P. GRAVES

HARVARD MEDICAL SCHOOL

OVARIAN ORGANOTHERAPY

Gynecologic Cases Representing Deviations in the Physiologic Pelvic Function and Their Treatment by Organotherapy; Varieties of the Disturbances, Clinical Manifestations, and the Management of these Cases; Several Case Reports.

IT is my purpose to demonstrate several cases typical of those gynecologic conditions that are amenable to ovarian organotherapy.

It is often claimed that in the present status of gynecologic science medicine has no place and that the specialty has developed almost exclusively into a branch of general surgery. This is to a certain extent true and seems likely to remain so in those departments which deal with new growths, destructive inflammatory processes, and conditions requiring mechanical reconstruction. In the surgical field most of the problems have been fairly satisfactorily worked out. There remains, however, a vast number of gynecologic cases which represent deviations in the physiologic pelvic functions. In the treatment of such cases surgery, like medicine, has proved, for the most part, a conspicuous failure, and it is exactly in this direction that the future progress of gynecology must lie. I refer especially to those disturbances which relate presumably to disorders of the ovarian function, and include such conditions as menorrhagia, amenorrhea, menstrual clotting of blood, dysmenorrhea, sterility, genital atrophy, and a long series of nervous and vasomotor manifestations which result from under- or overfunctioning of the genital glands. Up to the time of the discovery of the ovary as an organ

of internal secretion the understanding of these distrubances was involved in the deepest mystery. Studies of the secretory influence of the ovary in pelvic physiology threw some light on the subject, but the intricacy of the problem was only fully realized when it was found not only that the sex organs possess a very intimate relationship with the other endocrine glands, but that the other glands exert an important influence on the genital system independent of the ovaries, and may themselves be regarded to a greater or less degree as sex organs.

The enormous amount of experimental and clinical work done in endocrinology has up to the present time produced results of comparatively little practical significance, but what knowledge has been gained is of such nature that it promises much greater things for the future.

The ovary, among the glands of internal secretions, labors at a peculiar disadvantage, for the function of menstruation, in which from a practical standpoint we are chiefly interested, is almost exclusively a human attribute. In the study, therefore, of menstruation and all the numerous conditions associated with it we are limited to purely clinical observations with little aid from the more exact methods of laboratory and animal experimentation. One of the most important means that we at present have for studying human pelvic physiology consists in observing the influence of ovarian organotherapy on functional disturbances. This is admittedly an inaccurate method of research, for it involves many unavoidable chances for error. In addition to our theoretic ignorance of the nature of the active ovarian substance, we are handicapped by the wide differences that exist in individual human reaction to drugs. Moreover, statistical results of our work must depend on the verbal or written statements of patients who inevitably vary much in their interpretation of symptoms. These and other chances for error must be taken into account, and conclusions should not be too enthusiastically drawn one way or the other without weighing a large number of observations.

The first cases that I will bring to your attention represent the vasomotor disturbances that ensue after hysterectomy with or without the ablation of the ovaries. These manifestations

have been termed the "symptoms of the artificial menopause." They are analogous to but by no means identical with the natural menopause symptoms, for they are more constant, more distinctive, of shorter duration, and of more limited scope than the latter. They are also more amenable to ovarian therapy. In this particular field the efficacy of ovarian therapy can no longer be doubted, after making allowances for every possible error, for the results are so constant and so universally obtained by different practitioners and with different preparations that it may be confidently stated that there exists in the ovary a substance which specifically relieves ablation symptoms.

The fact that ovarian therapy sometimes fails in these cases does not necessarily weaken our conclusion, as is evidenced in the following case history:

The patient is a single woman of thirty-nine, who for a number of years has been employed as a physician's private secretary. She is naturally of rather a nervous, high-strung disposition, but is intelligent and sensible and keeps her nervous inclinations under good control. About three years ago I performed a hysterectomy with ablation of the ovaries for a chronic pelvic condition which had kept the patient ailing for several years. The convalescence was normal and the general condition of the patient improved by the operation. Ablation symptoms were, however, peculiarly severe and persistent. Instead of subsiding in two or three months, as is usually the case, they continued to be troublesome. During this time the patient consulted me for hot flushes and I prescribed an extract made from the whole ovary, a special preparation that I had found particularly efficacious for cases of this kind. She got little relief, however, from this prescription, and finding it too expensive, she bought from time to time nondescript extracts at the cheaper drugstores. She also tried several preparations prescribed by the physician for whom she worked, but all without relief. Finally, at the end of a year and a half, she consulted me again. The hot flushes had continued unabated and were now having a rather serious effect on her nerves. I had at this time begun trying out a new extract especially prepared for me, consisting of the dried residue of

pregnant ovaries from which the corpus luteum had been removed. The relief from this preparation was immediate and striking.

This case illustrates well an observation that I have frequently made in the treatment of ablation symptoms, namely, that patients exhibit idiosyncrasies to certain types of ovarian therapy. Thus some patients, as in the case just described, react specifically to the ovarian residue of pregnancy, others to the whole ovary, and still others to the corpus luteum. I can offer no adequate explanation for this. The milder cases of ablation symptoms yield to almost any of the better preparations, but in the severe cases it may be necessary to try several extracts before the right one is found.

The next case that I will present is similar to the first. These two are the worst cases of artificial menopause symptoms that I have had in recent years, and I wish to call your attention to them especially in order to demonstrate the possibilities of ovarian therapy.

This patient is a trained nurse, thirty-eight years old, much like the first case in physique and general temperament. She also was obliged to undergo a hysterectomy with ablation of both ovaries about a year and a half ago. The operation was followed by troublesome hot flushes which did not subside at the usual time. She had moved to a distant town, so that I had been unable to follow the case. She finally consulted me by letter, and I sent her at various times ovarian and lutein preparations, none of which had any appreciable effect. The dried ovarian residue which was so successful in the first case failed completely with this patient. Meanwhile the firm which had supplied me with the dried residue had prepared the same substance in ampule form for hypodermic injections. I first tried this form of treatment with this patient. Being a nurse, she was able to administer the injection herself. A recent letter reports an immediate satisfactory improvement in her symptoms.

In this case we see how a substance which when ingested in dried form was ineffective, at once produced the desired reaction when introduced in fluid form directly into the circulation.

This is as would be expected, for undoubtedly the active material of the ovarian substance must be deleteriously affected to a greater or less extent by the processes of digestion and absorption.

The next case illustrates the effect of ovarian therapy on an unusual form of vasomotor disturbance. The patient is a society woman of forty, from whom the pelvic organs were removed for uterine and ovarian disease about eight months ago. She made an excellent convalescence from the operation, but about three months later began to have hot flushes—a somewhat unusual circumstance, for they commonly appear soon after the operation. The flushes were, for the most part, of the ordinary type, but about once a day the patient suffered a sensation of great pressure in the head, accompanied by nausea. The eyes became suffused and there was mental confusion with inability to articulate. After several of these attacks, which came on periodically, the patient became alarmed and consulted me. Ovarian residue was given, with complete relief of the more serious symptoms and almost complete disappearance of hot flushes.

In this case we must consider the possibility of error on the ground that there may have been a hysteric element in the symptoms and a psychic influence in the treatment. This possibility cannot be entirely ruled out, but the patient is unusually intelligent and sensible and has not exhibited the slightest sign of hysteria in any other way. I am convinced that in this case the extract exerted a specific action on the symptoms.

These three cases illustrate the treatment of postoperative menopause symptoms and are perhaps more interesting to the surgeon than to the general practitioner. Similar results may be obtained in the treatment of the natural menopause disturbances. It has been my experience, however, that in the latter cases ovarian therapy acts with less promptness and surety, but is nevertheless a valuable remedy.

To the general practitioner the question of the value of ovarian therapy in menstrual disturbances is, perhaps, of chief interest. Theoretically one would expect it to have a specific influence on the protracted functional amenorrheas, but unfortunately this is not the case. I have prescribed the treatment for many patients

with this trouble, but have met with a conspicuous number of failures. Nevertheless an occasional success has been encouraging and suggests that a greater knowledge of the properties of the active ovarian substance and a more accurate information as to the causes of amenorrhea may in time lead to more successful treatment. Thus it frequently happens in treating cases of protracted amenorrhea that the administration of ovarian substance is promptly followed by a menstrual flow, but that continued treatment is without further effect. Such a case must be recorded as a failure, yet the primary effect certainly suggests that the ultimate inability to establish a catamenial rhythm may be due to ignorance as to the best method of administering the ovarian substance. Some cases of functional amenorrhea do not respond at all to ovarian therapy, and this, in my experience, is especially true when stigmata of other glandular involvement are present. Affections of the hypophysis and thyroid are most commonly represented in the polyglandular type of amenorrhea, in which case extracts from the corresponding gland are indicated in conjunction with ovarian substance.

When the amenorrhea is incomplete, that is to say, when it is interrupted by an occasional catamenial flow, the prospect of establishing a normal menstrual rhythm is favorable, as is well illustrated by the following case:

A school girl of eighteen consulted me in 1913 for infrequent menses, which appeared at intervals of about four months, accompanied by severe dysmenorrhea. For two or three years the patient had suffered from a constant sense of pelvic pressure. The menses had become infrequent three years before and at the same time the patient had begun to accumulate fat. Aside from the tendency to adiposity there was no other special indication of a polyglandular affection. The uterus was small, but not markedly infantile. An extract of the whole ovarian gland was prescribed and the patient directed to report by letter after each menstrual period. The directions were carried out minutely, and in a few months a regular menstrual rhythm had been established with intermenstrual periods of six weeks. The dysmenorrhea had almost completely disappeared, while the pelvic press-

ure, which had before been constant, was entirely relieved. After about a year I heard no more from the patient until June, 1917, when she again came under my care for chronic appendicitis, for which she was operated upon. At this time she stated that for the past three years the menses had, for the most part, been regular, with six-week intervals, but that occasionally they would be delayed for two or three months if she paid no attention to them. She kept a quantity of the ovarian extract on hand which she was accustomed to take when the menses did not appear on time. Under these circumstances menstruation would invariably appear within a week. The uterus at the time of the appendix operation was normally developed and the distinctive adipose look of the patient had disappeared.

The chance for error in this case is that the patient underwent a natural development coincident with and independent of the treatment. On the other hand, the response was so prompt and distinctive and has been so constant up to the present time that we may reasonably conclude that the symptoms were specifically influenced by the ovarian substance.

A similar case in my records is that of a girl of nineteen whose mother consulted me in June, 1917, with the statement that her daughter had been suffering from delayed menses, the periods averaging nine to ten days late. The delay was associated with physical depression and headaches. No opportunity was given for a pelvic examination, and I can only say that the physical appearance of that of the adipose type was rather more marked than in the previous case. In this case the pregnant ovarian residue was prescribed, to be taken for the ten days preceding the date on which the menstrual period should fall. Menstruation appeared at the proper time after the first ten days' treatment. This course of treatment was successfully repeated for two or three months, when a normal rhythm seemed to be established, so that now at the end of six months the patient menstruates regularly without the aid of medicine. She is in perfect health, the menstrual molimina having disappeared. The chance of misinterpretation in this case is that the effect on the menses may have been psychic. It is true that mental influences may affect the

menstrual function, either to inhibit it or to bring it on prematurely. In my experience, however, any mental influence sufficient to create so marked a change as was produced in this case would necessarily be the result of some profound emotion and would have acted deleteriously rather than beneficially.

The next case is one of scanty menstruation and dysmenorrhea associated with general physical depression. The patient is a young woman of twenty-one who works for a living. She did not menstruate until she was eighteen. For a year previous to the time of consultation the menses had been scanty and painful. Examination showed the patient to be overweight, with a uterus in marked anteflexion. Ovarian residue was prescribed to be taken continuously. Monthly reports were to be made after each period. The case was followed for four months, during which time dysmenorrhea disappeared and the menstrual flow gradually increased in amount. At the last report the patient stated that she felt entirely well and that the medicine had acted as a tonic.

I have noted a definite tonic effect from ovarian therapy in only a few instances. Possibly in this case the result was only psychic, that is to say, the general constitutional improvement due to relief of the menstrual disturbance was ascribed by the patient directly to the capsules which she was taking.

A special form of dysmenorrhea is that associated with clotting of the menstrual blood. The pain experienced by these patients is spasmodic and seems to be caused by the passage of the clots through the internal os. Certain cases of this kind seem to be amenable to ovarian therapy. The cases to be selected for treatment are not of the menorrhagic type, but rather those in which the flow is deficient or, at least, not excessive. The following is an example:

A married woman of thirty-nine, upon whom a reconstructive gynecologic operation had been performed several years previously, began to have clotting at her periods, with dysmenorrhea, headaches, and digestive disturbances. After seven or eight months she sought advice. Ovarian residue was prescribed to be taken for ten days preceding each catamenia. For three successive months the patient has reported a marked lessening of

pain and clotting, with corresponding improvement in headaches and indigestion.

A similar case is that of a woman of thirty-two, married five years without children, who consulted me in October, 1917, for clotting and dysmenorrhea. The treatment was prescribed for her as in the preceding case. Two monthly reports from this patient announce almost complete relief from clots and pain.

In the employment of ovarian therapy I have always been skeptical as to its efficacy in the treatment of sterility. I have, therefore, used it only occasionally for this complaint, and always with the statement to the patient that I had little faith in its accomplishing the desired results. Two cases have, however, very recently come to my notice in which there is at least a suggestion that ovarian therapy may have been instrumental in bringing about a pregnancy. Neither case is entirely conclusive, but I will present them for what they are worth. The first is that of a Jewish woman who called on me in December, 1917, bringing a friend whom she wished me to treat for sterility. She requested that I prescribe the medicine that I had given her and which she said had been entirely successful. I had quite forgotten the case, but on looking up her record found that in 1913 I had operated on her for multiple small fibroids and intestinal adhesions two years after her marriage. In June, 1916, she consulted me for sterility. I told her then that she probably would never have children, but prescribed lutein tablets (Hynson & Westcott) as a placebo. The patient stated that she very soon became pregnant and had a miscarriage at three months. She immediately became pregnant again and bore a child in June, 1917.

The second case is that of a woman of twenty-nine, married four years, who in April, 1917, consulted me for sterility and irregular menses. She occasionally had periods of amenorrhea lasting three or four months. Since the age of puberty there had always been more or less delay in the menses. Examination showed no pelvic abnormality. This was an ideal case for ovarian therapy, and accordingly a prescription was given for extract of the whole ovary (Armour's) to be taken continuously three times

daily. I did not see the patient again until September 17, 1917, when she made the following statement: For two months she had neglected to have the prescription filled. Soon after a menstrual period, which occurred in July 9th, she had procured the capsules and taken them faithfully for about a month, when she began to have bearing-down pains in the pelvis. Thinking that they were due to the medicine, she ceased to take it. Of late she noticed an occasional slight brownish discharge. For a week she had had daily nausea. There had been no menstruation since July 9th. Examination showed the patient to be about two and a half months pregnant.

In both these cases it is entirely possible that the occurrence of pregnancy following the ingestion of ovarian substance was an independent coincidence. I am, inclined, however, to regard both patients as having been potentially fertile, and that the ovarian substance acted to supply some functional deficiency in the pelvic physiology, which up to the time of treatment had been enough to prevent conception.

The nature of the functional deficiency and the manner of action of the ovarian substance are, with our present knowledge, only matters for conjecture.

In addition to the types of cases favorable for ovarian therapy, of which the foregoing are examples, I have had success in treating a certain number of patients who suffer from local discomfort resulting from circulatory disturbances of the external genitalia. The various conditions found in this type of case are usually the result of the atrophic changes which take place after the natural or artificial menopause. They include furunculosis vulvæ, kraurosis, pruritus, senile vulvovaginitis, and the vague forms of vulvar discomfort for which no well-defined pathologic cause can be detected. Not all of these cases are amenable to treatment, and my records show failures equal in number to successes. Nevertheless, some of the results with ovarian treatment are sufficiently striking to convince me that with a greater chemical and technical knowledge of the ovarian substance this will in time be an important field for organotherapy.

The rational basis for treating these circulatory cases is a

result of animal experimentation, which has demonstrated that the ingestion of ovarian substance produces a local hyperemia of the external genitalia in castrated animals. The immediate local relief which some patients receive after taking ovarian extracts indicates that a similar reaction takes place in human beings.

A perusal of the cases which I have reported will show that I have used the ovarian substance in three forms: 1. Ovarian residue, a dried preparation from the ovaries of pregnant animals, with the corpus luteum excluded (Parke, Davis). This is also put up in ampule form for hypodermic use. 2. Extract of the whole ovary (Armour's). 3. Extract of corpus luteum (lutein tablets of Hynson & Wescott). These three preparations have been, so far as my present experience goes, the most efficacious. The respective therapeutic value of the three forms has, in general, proved to be in the order named. This conclusion arrived at in a somewhat haphazard way from clinical observations is, however, not without rational theoretic confirmation. There is scientific evidence to show that the chief source of the ovarian internal secretion is in the so-called interstitial cells. These cells have their origin in the connective-tissue envelope of the follicles, and are developed both in the process of follicle atresia and in corpus luteum formation. Hence preparations from the ovarian stroma alone and from the corpus luteum alone both possess therapeutic value. It is probable, however, that the interstitial cells of the atretic follicles are more active than are the analogous cells of the corpus luteum. Preparations of the whole ovary, therefore, presumably would be more efficacious than those from the corpus luteum. This fact has been repeatedly shown in my own experience and in that of many other observers. It would seem to be corroborated by the fact that the advocates of corpus luteum therapy recommend enormous doses of lutein extracts for results which can readily be acquired with comparatively small quantities of the whole ovary.

The use of the ovarian residue of pregnant animals was the result of personal experimentation. In a series of cases treated with the corpus luteum of pregnancy it was found that the

substance had a decided toxic effect. As a control to this observation a series of cases was treated with the residue of the pregnant ovarian substance after the corpus luteum had been enucleated. The results with this preparation were striking and in some cases brilliant, toxic symptoms being entirely absent. This somewhat accidental discovery receives the support of the interstitial cell theory of the ovarian secretion, for during pregnancy follicle atresia is especially active, and hence there is at that time an unusual elaboration of the interstitial cells. It is, therefore, not surprising that the residue of pregnant ovaries has proved the most valuable therapeutic agent of any form that up to the present time has personally been tried. In my work on the ovarian residue I am indebted to Dr. J. F. Grant for valuable co-operation and suggestions.

CLINIC OF DR. EDWIN A. LOCKE

BOSTON CITY HOSPITAL

OSTEITIS DEFORMANS WITH SARCOMA OF THE HUMERUS

x-Ray Appearances in the Bones; Course and Prognosis; Differential Diagnosis; Symptoms; Treatment.

October 18, 1917.

THE case which we are to discuss this morning is an unusually interesting one not only as regards the primary disease but also the complicating condition.

Mr. A., to whom the case was assigned in the wards, will give us a brief history.

The patient, W. S., a violinist aged sixty-two, entered the hospital October 8, 1917, complaining of a painful swelling of the right elbow of eighteen months' duration.

Family History.—Negative.

Personal History.—Always strong and well. No illness except the diseases of childhood until the present illness. Always a heavy smoker. Very moderate drinker. Denies venereal. In 1892 fell and broke left patella. Of late years increasing deafness, and occasionally moderate sensations of fluttering in the region of the heart. No other cardiac symptoms. No respiratory, gastric, or renal symptoms. Weight for thirty years 180 pounds, now 160.

Present Illness.—For the past eighteen months the patient has suffered from pain in the region of the right elbow. It began as a slight and variable tingling in the joint, later becoming burning, and finally stabbing and paroxysmal. For the past few months the pain has been of a dull character, but constant and very severe, worse with any motion of the elbow. At first confined to the joint region, latterly the pains have been

felt in the upper forearm and lower arm. Any motion at the elbow-joint has become less and less because of pain. No swelling was noted until about three months ago, since which time it has increased rapidly and has been considerably inflamed. The enlargement was first noted in the region of the olecranon.

Physical Examination.—A few moderately enlarged lymph-nodes in the anterior cervical region, not tender. The heart very slightly enlarged to the left; no murmurs; sounds of good quality; A_2 slightly accentuated. Peripheral arteries palpable and tortuous. Blood-pressure $\frac{120}{85}$. The right elbow is enlarged to about twice its normal size, with the greatest prominence posteriorly, slightly reddened over the outer portion where there is definite fluctuation. Very acute sensitiveness to pressure; the slightest passive motion gives intense pain.

Blood: Hemoglobin, 85 per cent. Red count, 4,320,000 per cubic millimeter. Leukocytes, 8400 per cubic millimeter. Wassermann test negative.

Urine normal except for slightest possible trace of albumin. Temperature, pulse, and respiration normal.

Dr. Locke: Briefly stated, we have here a man of sixty-two years whose past history is negative and who during the past eighteen months has suffered from a slowly increasing and painful swelling of the right elbow. Your physical examination is negative except for the condition in the elbow and the evidence of arteriosclerosis. What conditions have you considered as explaining the swelling in the right arm?

Mr. A.: I have considered gout, chronic arthritis, Charcot's joint, tuberculosis, osteomyelitis, syphilitic arthritis, and malignant disease.

Dr. Locke: Before discussing the diagnosis I want to show you the *x*-rays of the affected arm. The appearances are quite extraordinary. Note first that the humerus is fairly evenly enlarged to nearly twice its normal diameter, but the lime salts are strikingly lacking. The normal structure is almost entirely lost. The medullary portion is fairly marked; the cortex is unevenly striated, with here and there coarse trabeculæ.

At its distal end for a distance of about 3 inches the bone is

represented by a mere shell very much broadened, honeycombed, and irregular. There is hardly a semblance of a joint cavity. Likewise the structure of the epiphyseal portion of the radius and ulna present changes of exactly similar nature except that there seems to be little if any enlargement. The diaphysis of these two bones for a distance of 3 or 4 inches shows a marked degree of absorption, though the size is unchanged and considerable normal structure is preserved. The calcified arteries are plainly visible.

Will you now discuss the possible diagnoses which you mentioned?

Mr. A.: There is no evidence for gout either in the history or physical examination. The patient has had no symptoms suggesting this disease and I can find no tophi. The *x*-ray is negative so far as gout is concerned. Chronic arthritis seems more probable.

Dr. Locke: If this is chronic arthritis it must be one of two forms, namely, osteo-arthritis or infectious arthritis. So far as the former is concerned it would be very unusual to have an osteo-arthritis confined to an elbow-joint. It is much more common in the knee, hip, spine, or small bones of the feet and hands. Furthermore, the joint does not present any of the characteristics of this condition. Finally, the *x*-ray gives a picture entirely unlike osteo-arthritis.

So far as infectious arthritis is concerned it is sufficient to say that the patient has had no general symptoms of an infection, there are no heart complications, there is no evidence of a source of infection, and locally the signs of inflammation, except for pain, tenderness over a limited area, and slight redness over a small area of the surface, are wanting. The *x*-ray does not show the usual features of this type of joint disease.

Charcot's joint was the next condition mentioned.

Mr. A.: I believe this disease can be readily ruled out. There is no tabes, syringomyelia, or other chronic disease of the spinal cord here to which Charcot's joint is always secondary. The pain and tenderness are more extreme than is ever seen in this joint disease.

DR. LOCKE: The radiographs again give us valuable assistance. The *x*-ray appearances in Charcot's joint are very definite. Most characteristic of all is a degree of hypertrophy greater than is found in any other joint condition which I can recall. Not only does one see large excrescences on the bones forming the joint, but the capsule contains relatively large, free bodies which are densely calcified.

MR. A.: The advanced age of the patient is very much against the diagnosis of tuberculosis. There is no evidence of tuberculosis elsewhere in the body. With this disease there should be some fever reaction, the pain and acute tenderness would not be so extreme, and there are no sinuses which after a period of eighteen months might be present, and the roentgenograms do not show appearances characteristic of tuberculosis.

Osteomyelitis is likewise rare at this patient's age, there is no evident primary focus so commonly present, and fever is absent.

DR. LOCKE: Would you not expect a leukocytosis if this were a case of osteomyelitis?

MR. A.: Yes.

DR. LOCKE: There are no general symptoms of a localized infection. The *x*-ray appearances might conceivably be explained as resulting from an infectious process involving the bones and joint. Schuchardt describes an unusual chronic infection of the bones ("osteomyelitis centralis chronica") which is seen in mature years. If the focus in the long bone is near the joint the latter is often involved. It seems to me, however, that osteomyelitis may safely be excluded.

MR. A.: Syphilitic arthritis need not be discussed, as there is no history of a luetic infection and the patient shows no evidences of the disease. The Wassermann test is negative.

DR. LOCKE: Syphilis of the joints is a relatively rare affection, especially in the acquired form. In the tertiary stages joint complications occasionally develop, and, I believe, are almost never recognized as luetic. Two types occur: (1) The so-called "perisynovial gummatous arthritis" usually affecting the knee-joint, but occasionally the elbow, the periarticular tissue being invaded by gummatous deposits. It may simulate closely joint

tuberculosis. (2) A rarer form, which is really an osteo-arthritis, is also most common in the knee. The resulting enlargement of the bones may be mistaken for osteosarcoma.

What form of malignant disease had you in mind?

MR. A.: Primary carcinoma of the bone is very rare, and secondary carcinoma can be discarded, as there is no primary focus which after so long a period would be evident. If the tumor is a malignant growth I had considered it a sarcoma of some form. Its gradual growth with increasing pain and loss of function of the joint is characteristic of sarcoma. The general appearance of the tumor is typical also.

DR. LOCKE: I should consider the extensive destructive process in the bones and joint as indicated by the roentgenograms as typical of what is often seen in sarcoma. It seems to me the most probable diagnosis is sarcoma of the humerus.

Close observation should have led you to note certain other appearances in this patient which are very obvious and which are pathognomonic of another disease. The malady is a very common one and so striking in the deformities which it invariably presents that it cannot be overlooked. It is my experience that the condition is but seldom recognized. Did you notice any deformities?

MR. A.: His legs are somewhat bowed, but I thought it was due to old age.

DR. LOCKE: Yes, the legs are evenly and markedly bowed throughout, the curve being outward and forward. The bowing is perhaps more noticeable in the lower legs than in the thighs. Palpation of the thighs indicates a considerable thickening of the femora and they are much curved. The tibiæ are enormous, being at least twice their normal size, almost cylindric, and their surface very uneven, the normal markings being entirely lost. The left shows greater changes than the right. Both knees are very massive, but motion is reasonably free. There are no objective signs of inflammation. The feet and ankles are not noticeably abnormal. The pelvis is extremely broad, and if you will examine the bones you will see that they are very massive and irregular.

As I test the motion in his spine you will see that it is almost rigid throughout. The lumbar portion has lost entirely its normal curve and the dorsal presents a very definite kyphosis.

The chest may at first glance not strike you as unusual. Look, however, at its general shape. It is unusually deep, but not only is the anterior posterior diameter increased but the thorax looks as though it had been compressed laterally. It is actually quadrilateral, in sharp contrast to the rounded chest seen in emphysema. If you will examine the bones of the thorax you will find that they are all significantly augmented in size. If I ask the patient to take a deep breath it will be evident that the breathing is diaphragmatic in type, the ribs scarcely moving as in normal respiration.

The normal curves of the clavicles are grossly accentuated and they are much enlarged and rounded. Equally great changes and of the same nature are to be found in the scapulæ. This patient fails to show what is so striking in many, namely, an appearance as though the head were set almost directly on the shoulder girdle. In some the chin is carried forward and practically rests on the sternum, from which it can be raised only an inch or two.

I am able to demonstrate more than the usual alterations in the bones of his upper extremities. The deformities are about equal on the two sides. The humeri are bowed anteriorly throughout their entire length, and as I feel them it is evident that they are much larger than normal. The bones of the forearms do not feel enlarged, but you will clearly see a considerable outward bending. Pronation is complete, but supination is greatly limited. The hands appear unchanged.

The calvarium looks a trifle larger than normal, but the measurements made in the ward are within normal limits. You will all agree that the lower jaw is very large and projects forward (prognathism).

If I now have the patient stand, many of these changes will be emphasized. It also gives me an opportunity of calling your attention to certain important characteristics of the disease. In the first place you will observe that the posture is quite unique.

He stands with the feet strongly everted, so that they are at about a right angle and with one considerably in advance of the other. This position of the feet is presumably taken in order to preserve a proper balance. The bowing of the legs is much more evident in the standing position. The internal condyles are about 20 cm. apart. Marked flexion of the pelvis on the thighs throws the trunk forward, which, together with the forward curving of the spine, gives a striking stooping posture.

Particularly noticeable is the contraction of the abdomen. It is small and protruding with a deep transverse groove at the level of the navel due to the fact that the costal edge is almost resting on the crests of the ilia. In consequence of the forward position of the trunk the arms appear unusually long, the hands reaching to the knees. This suggests the semblance of an anthropoid ape so often mentioned.

The patient's gait as you see him walk is peculiarly stiff and waddling. With each step the pelvis is tilted and the leg swung forward.

Considering the changes which I have just demonstrated in the skeleton I feel sure it will be possible to elicit from the patient some further history bearing on these changes.

(Addressing patient): Your legs are considerably bowed. Have you not noticed this before entrance to the hospital?

PATIENT: About eleven years ago my son called my attention to the fact that my legs were slightly bowed, and for several years following I think the deformities increased somewhat, but for the past eight or nine years I am sure no further changes have taken place. The left has always been more deformed than the right. The condition, however, has never bothered me and I have paid very little attention to it.

DR. LOCKE: Have you noted any changes of a similar nature in the thighs or pelvis?

PATIENT: I am sure no changes have taken place.

DR. LOCKE: Have you had any pains in the legs?

PATIENT: Not in recent years. Some years ago I occasionally had dull and rather severe pain in the lower legs which seemed to be in the bones.

DR. LOCKE: Have you ever had any localized swelling or redness over the bones of the lower legs, or has there been any tenderness?

PATIENT: No, but if I injure my shin in any way it seems unusually sore and for a long time.

DR. LOCKE: Have you ever had cramps in your legs?

PATIENT: Not in recent years, but some six or eight years ago I frequently had very severe agonizing cramps in the calves of my legs after going to bed at night.

DR. LOCKE: Have you any opinion as to the cause of these cramps?

PATIENT: They usually came on at night after I had been on my feet all day and was very tired.

DR. LOCKE: Were these cramps severe?

PATIENT: At times they were very severe, forcing me to bound out of bed. I could get some relief from rubbing the muscles, but more from walking about on the cold floor.

DR. LOCKE: Have you noticed any difference in your gait or stiffness in your joints?

PATIENT: I can walk about as usual, although I am perhaps a little more clumsy and stiff. The joints all over my body are occasionally stiff also, but I have attributed this to my age.

DR. LOCKE: Have you lost any height?

PATIENT: I do not think so. I cannot recall exactly my former height.

DR. LOCKE: It is obvious that from the patient's position in standing he must have lost at least 2 or 3 inches. (To patient): Have you been obliged to increase the size of your hat in the past ten or fifteen years?

PATIENT: No, I wear the same sized hat now as when a young man, namely, $6\frac{7}{8}$.

DR. LOCKE: Have you noted any change in the lower jaw?

PATIENT: Yes, for many years I have noticed that the lower jaw was somewhat more prominent, and my family have called my attention to it.

DR. LOCKE: I have taken the time to ask these questions before you because it illustrates so characteristically the insidious

course of the disease. The changes in the skeleton are so gradual and often without pain that the patient is entirely unconscious of them until an extreme stage of the disease is reached. During the past fifteen years I have had the opportunity of examining a considerable number of these cases, and in almost every instance the characteristic changes have been first noted by some member of the family who has called the patient's attention to them.

x-RAY APPEARANCES IN THE BONES

I shall now show you roentgenograms of the entire skeleton, calling your attention to the type of changes manifested. First, let us take a lateral *x*-ray of the skull. The appearances shown are most surprising and striking. You will see first that there is an enormous thickening of the entire calvarium, the bone in its thickest part, which is in the occipital region, being fully $\frac{3}{4}$ inch. Although the surface is somewhat uneven the bone is, on the whole, of fairly uniform thickness. In contrast to the normal skull as shown in the *x*-ray you will see that its structure is entirely changed. The inner half is perhaps more dense than normal, but the outer portion is thin and shows an entirely abnormal appearance. At the very cortex the calcium salts are in places entirely wanting. In no part, however, is the bone substance entirely absent over large areas, as is so characteristic of the appearances seen in syphilis and certain of the tumors.

So far as the remainder of the skull is concerned you will see that everywhere the bone seems to be increased in density and appears massive. This is equally true of the interior maxillary bone.

Next let us take the tibiæ, which show most extraordinary appearances. In the first place you will see that the entire bone is involved, the changes being almost equally evident in all parts. Second, the bone in each case shows a broad curve throughout. Third, the bones are enormously thickened, in case of the left to nearly twice the normal diameter. Fourth, the normal markings which differentiate the medulla from the cortex have to a great extent disappeared. Fifth, the thickening appears to be greatest on the convex surface. Sixth, the outline

of the bone is especially on the convex surface particularly irregular and wavy. Seventh, the minute structure of the bone appears absolutely abnormal, scarcely any of the normal markings being present. In places, especially at the cortex, the bone seems thin and evidently contains very little lime salts, while in other places the density seems to be increased. Eighth, in the epiphyseal

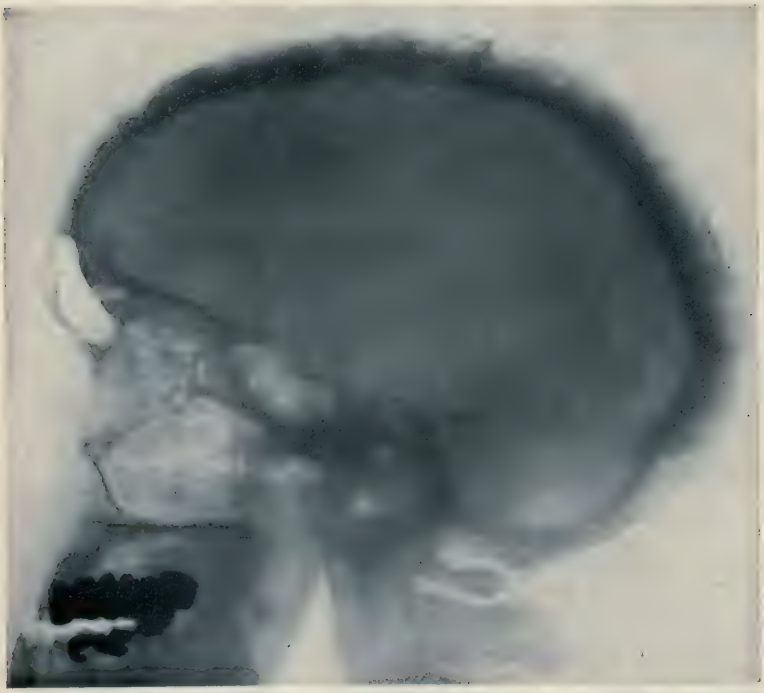

Fig. 99.—Lateral view of skull. Note the general increase in the osseous structures, especially the great thickening of the calvarium and the alterations in the outer table.

portion the bone seems very much increased in size and the internal markings altered strikingly. There is very coarse trabecular marking. The articular surface seems to be unaffected. In a few places you see small oval areas lying lengthwise in the shaft of the bones from 1 to 2 cm. in length which represent small bone cysts. These are quite commonly found in this disease.

On looking at these *x*-rays one is immediately struck with the

clearness with which the arteries of the legs are seen. They appear very tortuous, and from the clearness with which they are seen it is fair to assume that they are extensively calcified. I shall call your attention to this same condition in the *x*-ray of the thighs and arms.

Fig. 100.—*x*-Ray of tumor of left elbow. The humerus is thickened to twice its normal size, and in its distal portion the bone is almost completely destroyed. Hardly any normal joint muscles remain.

The fibulæ are not well shown in these *x*-rays, but it is clear that the involvement of these bones, although of the same type, is much less extensive and marked. The patellæ show considerable change.

If we now examine the bones of the feet we observe rather general changes of the type described above in the os calcis and astragalus in each foot, and also in one or two of the tarsal bones. Alterations of about the same grade as exist in the right tibia are

Fig. 101.—Case shown in clinic. Note characteristics described in text.

evident in the femora. I am sure you are surprised by the appearances of the bones of the pelvis. Not only is the internal structure entirely altered, but the bone everywhere seems greatly thickened. Even in the vertebræ one finds evidences of moderate changes.

The thorax likewise shows unmistakable variations from the normal. A few of the ribs are noticeably gross, and in places the structure of the bones is quite similar to that described in the tibiæ. The most marked changes are seen in the clavicles and scapulæ. Even more marked are those in the humeri, both of which are nearly twice the normal thickness and are moderately curved anteriorly. The bones of the lower arm are only slightly changed, while those of the hand are normal except for one or two of the carpal row.

DISCUSSION

We have before us, then, a patient whose history, general skeletal deformities, and the *x*-ray appearances of the bones are very typical of osteitis deformans (Paget's disease). I will give you references to a few of the best general articles on the subject:

Paget: Med.-Chirurg. Trans. Med. Chirurg. Soc., London, 2d series, vol. xlii, 1876, p. 38.

Sternberg: Nothnagel's Specielle Pathologie u. Therapie, Bd. 7, T. 2, Abt. 2, s. 64, 1899.

Packard, Steele, and Kirkbride: Amer. Jour. Med. Sci., cxxii, 559, 1901, and Trans. Assoc. Amer. Phys., xvi, p. 666.

Schirmer: Centralblatt f. d. Grenzgebiete d. Med. u. Chir., Bd. 11, Nos. 15-19.

DaCosta, Funk, Bergeim, and Hawk: Publications from The Jefferson Medical College and Hospital, vol. vi, 1915, p. 1.

The term "osteitis deformans" was first suggested by Czerny in 1873. The condition described under this name was a local inflammatory process confined to the lower portion of one tibia and fibula in a young man of twenty-two. From the description of the case given by Czerny it is clear that the condition which he describes is entirely different from the disease now commonly known by that name.

A few years later, namely, in 1876, Paget reported before the Medico-Chirurgical Society of London a series of 5 cases under the title, "On a Form of Chronic Inflammation of Bones (Osteitis Deformans)." This paper is one of the classics in medicine and I would strongly advise all of you to read it. It is quite remarkable for the accuracy in observation and the masterly description of the diseased condition. It is fair to say that the history of the

Fig. 102.—Right radius and ulna. Ulna normal. Radius shows typical bowing and alterations in structure throughout the diaphysis. Articular surfaces unchanged.

disease begins with this paper by Sir James Paget. Thirteen years later this same author stated that he had subsequently seen 18 cases, making a total of 23. Since this time a voluminous literature on the subject has accumulated, but notwithstanding the many studies made, surprisingly little has been added to the original description by Paget.

Incidence: The original statement of Paget that the disease is a rare one would seem to be borne out by the fact that to date approximately only 250 cases have appeared in the literature. Hurwitz found only 3 cases among 30,000 medical admissions to the Johns Hopkins Hospital, and DaCosta, Funk, Bergeim, and Hawk only 3 cases among 38,000 admissions to the new Jefferson Hospital in Philadelphia. I cannot agree, however, that the condition is so rare as these figures might indicate, for my own experience includes nearly 50 personally observed cases. Each year several are seen in the wards of this hospital.

Etiology. — Many theories have from time to time been ad-

Fig. 103.—Lower legs. In left tibia observe the bowing and immense thickening throughout, complete alteration in structure; wavy indistinct outline along anterior surface, indistinct outline of medulla, and cyst formation. Right tibia shows earlier changes of the same type.

vanced to explain the origin of this disease. Among these causes are gout, chronic rheumatism, syphilis, trauma, neurotrophic condition, disturbance of the secretion in the ductless glands, and bacterial infection. Positive proof is uniformly lacking that any one of these is the cause of the changes in the bones, and I believe it can be reasonably stated that the etiology is unknown. In my own series of cases I have been particularly struck with the fact that they have uniformly shown an extreme degree of arteriosclerosis which I can hardly conceive as appearing in so large a series without some etiologic significance. Your attention was called to the high degree of sclerosis in the arteries of the arms and legs of this patient as indicated in the *x*-ray plates. It is my conviction that the disease is in some way dependent upon trophic changes which result from extreme arteriosclerosis.

Osteitis deformans is usually spoken of as a disease of old age, but a study of the cases in the literature indicates that in a majority of instances it begins in early middle life. Several instances of cases beginning under twenty have recently been recorded. Its course is usually a very long one, frequently covering thirty or forty years, and as the patient usually comes under observation only when the disease is well developed, which frequently means after a period of from ten to twenty years, it is easy to appreciate that the impression should be given of a disease of old age.

Heredity seems to play a very definite part. A considerable number of instances are now recorded where a member of the previous generation suffered from the same malady. Among the cases which I have observed approximately 20 per cent. give a history of the same condition having existed in one of their parents.

Males seem to be about twice as frequently afflicted as females.

Pathology.—The essential changes taking place in the bones may be summarized as follows:

1. The process usually begins in the long bones of the lower legs, although not infrequently its first appearance is in the skull. In the late stages of the disease practically the whole skeleton may be involved.

2. The individual affected bones are much enlarged, and in the case of the long bones are more or less cylindric and show the process evenly distributed throughout the entire shaft. In a few instances individual bones are seen in the *x*-ray where the changes are confined to a third or more of the bone, giving the appearance as though the shaft were gradually being invaded. The surface is slightly rough and uneven, but never shows large exostoses.

3. Bowing of the entire shaft of the long bones is marked and characteristic.

4. For the most part the bones are soft and cut easily with a knife, although in certain areas and especially in the late stages of the disease one finds areas of ivory hardness.

5. The cut surface shows a coarse, trabecular structure alternating with large and small areas of denser bone tissue. When the process is well advanced the normal appearance of the cut surface is entirely lost. The bones seem very rich in blood.

6. The marrow space is early encroached on and frequently entirely obliterated.

7. The periosteum is not, as a rule, thickened, but is often slightly adherent.

8. Small cysts are frequently seen.

9. The articular cartilages are, as a rule, preserved and caries and necroses are never present.

The process going on in the bones is a double one. First, there is a resorption of old bone; second, an apposition of new "fibro-osseous" tissue. From *x*-ray studies of cases over a long period of years it seems evident to me that the two processes go hand in hand, although probably the resorption of old bone is the initial one. The apposition of new bone takes place largely from the periosteum, although the marrow contributes also.

Careful chemical analyses of various bones in 4 of my cases have given somewhat varying results which are difficult to interpret. These analyses have all shown a great increase in the percentage of organic matter with a marked diminution in the percentage of lime and magnesium and a slight decrease in the percentage of phosphorus. The only trustworthy metabolism ex-

periments are those recorded by DaCosta, Funk, Bergeim, and Hawk (2 cases). They find a pronounced detention of calcium, magnesium, and phosphorus, with a pronounced loss of sulphur, which findings they interpret as indicating a stimulated osseous or osteoid formation accompanying the resorption of the highly sulphurized organic matrix.

Symptomatology.—The disease shows quite extreme variations both in the rapidity of its development and its clinical manifestations, but, on the whole, the clinical picture is one of unusual definiteness. Only in its early stages should the disease ever be confused with any other condition.

The roentgenograms particularly show structural changes, deformities, and an order of involvement of the bones which is unique.

The onset is invariably insidious, the patient being unable to give exact statement as to the duration. As a rule neither

Fig. 104.—Reproduction of a tibia of an advanced case of osteitis deformans. Compare with *x*-ray of tibia (Fig. 103). The bone is involved in its upper two-thirds only, the line of demarcation between the diseased and normal bone being well defined. In the diseased portion the striking features are the enormous thickening, greater in the anterior portion, and with alterations in structure, the slight anterior bowing, and the increase in blood.

pain nor deformity is the first symptom noted. In a vast majority of cases the first signs observed are objective and consist in a bowing of the lower legs. The process which so often begins in the tibiæ gradually involves the rest of the skeleton almost always in a manner which may be called irregularly symmetric. In a few cases given in the literature alterations in the calvarium seem to antedate by a considerable period, often years, those in other parts of the skeleton (hyperostosis cranii). In a vast majority of cases, however, where the process is well developed the axial bones are the ones most involved. *x*-Ray studies of cases of osteitis deformans demonstrate clearly that the process may begin in several bones at the same time. The characteristic bowing of the long bones is admirably illustrated by the case which you have seen today. The arching is always in the direction of the natural curve of the bone.

The attitude of a case of osteitis deformans on standing I have demonstrated to you this morning in considerable detail. You have seen that it is both unique and grotesque. So characteristic is it that in well-developed cases inspection is quite sufficient for diagnosis. The head is, as a rule, enormous, the enlargement being confined largely to the calvarium. It is frequently carried forward with the chin almost touching the chest. The small quadrilateral thorax is held rigidly during respiration and the bones seem massive. The spine is curved forward, bringing the costal border almost in contact with the crests of the ilia. The abdomen is, in consequence, small and protruding, and usually with a deep transverse groove. In contrast to the relatively small trunk the pelvis is enormously widened and seems out of all proportion to the rest of the body. The legs are bowed outward and forward and in extreme cases are actually crossed. On standing, the feet are everted to approximately an angle of 90 degrees, and there is a considerable degree of flexion in the hip-joints, knees, and ankles. Although much less frequently seen, the arms may also present quite marked changes, the upper arms being curved forward and the forearms outward and forward. The gait, as you have seen, is strangely labored and waddling.

Pain, which is present in a considerable majority of cases, is a most annoying symptom. As it coincides with the seat of bone changes it is most common in the legs, although I have frequently seen it in the arms and back. The character of the pain is variable. Most commonly it is described as an intense, dull, rheumatic pain which seems to be in the bones. Occasionally it is sharp and lancinating. An individual with osteitis deformans may reach an advanced stage without any pain whatsoever. With the vast majority the intensity of the pain diminishes materially with the advance of the process in the bones. Intense cramps in the muscles of the lower legs are common.

I have observed very constantly in these cases general failing health, and they frequently present the picture of premature senility. Although the joints are seldom involved in the sense of any actual arthritis being present, patients very frequently complain that all their joints are stiff.

Undoubtedly a *mono-osteitic form* of this disease occurs, although it must be considered an excessively rare condition. Dr. Hurwitz, of the Peter Bent Brigham Hospital, has recently published an excellent paper on this subject reporting one of his own and collecting others from the literature. No case of this type should be accepted as an example of Paget's disease unless the diagnosis is confirmed by histologic or radiographic examination, for the condition may be easily confused with syphilis or malignant growth of a bone. Several cases which were apparently the mono-osteitic form have come to my notice. In each instance radiographs of the entire skeleton have shown typical osteitis in multiple bone.

Complications are not a striking feature of this disease. Occasionally I have seen severe neuralgia develop, but with no greater frequency than in the case of other chronic debilitating diseases. Cardiovascular changes are perhaps most commonly associated with the condition. The frequency with which a high degree of arteriosclerosis occurs has already been emphasized. Undoubtedly as a result of this condition myocarditis is frequently found. In the late stages of the disease cardiac dilatation is so common as to be almost considered the rule.

Fractures of the affected bone are far less common than in osteomalacia, a fact entirely in accord with the striking difference in the process in the two diseases. Surprisingly few examples of fracture are found in the literature of this subject. Among my own cases I have seen a considerable number, usually of the tibia, femur, or long bone of the arm. The explanation of the fact that fractures of the diseased bones do not occur more frequently is explained by the extensive formation of the so-called "fibro-osseous tissue" which plays such an important part in the pathology of the disease. I have personally seen some eight or ten examples of fractures, usually spontaneous, in patients suffering from osteitis deformans, and in each instance the bone has healed promptly and completely. Indeed, in a few cases the healing has seemed even more prompt than in the case of normal bone. Although the disease itself practically never involves the joints, a moderate degree of osteo-arthritis, especially in the knee, hip, or elbow, is a fairly frequent accompaniment. Localized periostitis, usually of the tibia, is very frequently met with. Insanity has been recorded in a few cases. Paget himself emphasized the frequency with which malignant disease either of the bone or other tissues complicates osteitis—8 of his own cases were traced to the end, and 5 died of malignant disease. Many other examples of such an association are recorded. It would seem reasonable that sarcomatous growths should develop in the bone where, as a result of the extraordinary changes, the normal cellular activity must be greatly disturbed.

Course and Prognosis.—The course of the disease is, as a rule, very protracted, ranging from ten to forty years. The activity of the process in the bones very often seems to become quiescent after a period of ten or twenty years. I can recall several instances where the disease has not appeared to progress during a period of ten or twelve years and where the *x*-rays have failed to show any progress in the alteration. Death never results from the osteitis, but from some intercurrent disease, most frequently of the cardiovascular system.

Differential Diagnosis.—This seldom if ever presents any difficulties unless it be in the very early stages of osteitis defor-

mans when the characteristics of the disease are not fully developed.

Localized hyperostoses may rarely be confused with Paget's disease, especially those of luetic origin. Hyperostosis affects only a portion of a single bone, most often giving it a spindle shape locally, but not deforming the entire bone as in the case of Paget's disease. The *x*-ray indicates a periosteal growth, usually a spindle-shaped enlargement of the bone, and, so far as the finer structure is concerned, only an increase in the normal structures or increased density.

Rickets possesses only the most superficial resemblance to osteitis deformans. The former is a disease of growing bones in early life. It is not progressive and the osseous changes are not so general. The process affects the epiphyseal portions particularly, which are short and small, and the curve unlike osteitis deformans. The *x*-ray appearances in the two conditions are entirely dissimilar.

Osteomalacia under some circumstances presents a picture more closely resembling osteitis deformans than any other condition. Osteomalacia occurs most commonly in young women, especially after childbirth. Spontaneous fractures are more common. Anatomically the changes in the bones are quite unlike those found in osteitis. The bones are thin and show a marked process of atrophy. The bowing is angular and irregular, as is also the enlargement when present. In the case of this disease the process in the bones is essentially one of decalcification, whereas in osteitis deformans the predominant process is one of new bone formation with an actual deposit of lime salt.

Osteoporosis senilis need hardly be mentioned. Here there is no hypertrophy of bone, but rather an atrophy and deformity occurs only as a result of fracture and callous formation. Pain is wanting.

Secondary hypertrophic osteo-arthropathy (ostéoarthropathie hypertrophiante pneumique, Mariés) in its later stages may, as in one example which I recall, show changes in the long bones not unlike osteitis deformans. In this instance the bones were enormously thickened and the finer structure as shown in the

x-ray was very suggestive of osteitis deformans. The bones, however, were not curved. Except in these late stages the process in the long bones is strictly confined to the cortex, the new bone being laid down as a definite layer just beneath the periosteum. The clubbing of the fingers and toes and the cylindric enlargement of the lower legs and forearms are signs which in themselves are sufficient to establish a diagnosis of osteo-arthropathy as against osteitis deformans.

Therapy.—There is no specific treatment.

NOTE.—The patient left the hospital on October 21st and on November 23d he entered the Peter Bent Brigham Hospital on the service of Dr. John Homans, 2d. During the interval the tumor had increased considerably in size and the symptoms were more severe. A diagnosis of sarcoma of the humerus was made by Dr. Homans, who operated December 12th, amputating the arm and resecting the axilla. The tumor on section was found to be a new growth of the femur, the central portion having broken down and being filled with a bloody fluid. Histologic examination showed the structure typical of spindle-celled sarcoma (Dr. Wolbach).

CLINIC OF DR. CHARLES J. WHITE

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PREMATURE LOSS OF HAIR

Infectious Diseases; Diagnoses; Effects of Systemic Toxemias on the Scalp; x-Ray Alopecia; Hygiene of the Hair; Management and Treatment of the Different Varieties of Alopecia, etc.

GENTLEMEN: It has been said from time to time by various other specialists in medicine that dermatologists often write upon trivial themes. This may be true at times from the viewpoint of physicians who are not interested in scientific cutaneous medicine; but I assure you that there are many clinical themes which may seem of slight importance to a man in his capacity as an operating surgeon, for instance, but let that same man be affected by certain skin diseases and he will often quickly change his mind and come running to the dermatologist for help and advice. Such an assertion I base on repeated experience. Such a theme is premature loss of hair, a loss which may result from an infectious disease, from alopecia areata, from the application of *x*-rays, but principally from the combination of heredity and subsequent infection with the germ of seborrhea.

Infectious Diseases.—If an individual acquires an infectious disease, be it pneumonia, scarlatina, measles, or what not, he frequently notes a subsequent loss of hair which is usually generalized in distribution and may be slight in amount or may be of such a degree as to alarm his peace of mind. There does not seem to be any hard-and-fast rule in the frequency of this alopecia, but let me state that it occurs, fortunately, in the decided minority of instances. There is, however, a strikingly correct observance of the interval of time elapsing between the onset

of the fever of the disease and the subsequent initial loss of hair. One might even say that one could tell a patient the exact date of the incidence of his previous constitutional symptoms if one were told the precise day on which the hair began to fall. This interim is practically three months.

In this connection allow me to relate a curious illustration of this phenomenon. A young girl was attacked by erysipelas of the scalp which in the course of the disease involved the anterior half of the head. A few days after the subsidence of the infection the hairs began to fall from the involved portion of the scalp and eventually practically totally disappeared; but three months from the time when she fell ill the hair began to disappear from the remaining portions of the head. Here we had the rare opportunity of observing the local as well as the constitutional effects of a toxin.

This local effect of infection is, of course, best observed in cases of alopecia due to infection with the ringworm and favic organisms, *i. e.*, Tinea tricophytina and Tinea favosa; but here the loss of hair is due not to toxins, but to the actual consumption of the hair by the plants. In ringworm two varieties of hyphomycetes are observed, the microsporon and the megalosporon. In the former only children up to the age of fourteen are affected and the result is one or more sharply bounded, rounded areas of apparent baldness in which one observes the scalp covered with ashen gray scales from which emerge a relatively small number of hairs perhaps $\frac{1}{8}$ inch in length. If one pulls out one of these hairs and holds it up to the light one will note its apparent increase in diameter due to the surrounding envelope of plant growth. In the baldness due to the large-spored variety all ages may be affected, but in Boston this type exists in not more than 10 per cent. of the cases. Here the area is ill-defined and of irregular shape. The scalp is reddened and the overlying scales are few in number. There are no broken-off hairs and islands of perfectly normal hairs may persist in the midst of the affected areas. In favus the loss of hair does not occur in any prescribed localized patch—it is totally irregular, it has no definite shape. One sees merely the absence of hairs, a

yellowish, adherent, sparse scaling and a darkly reddened skin. Occasionally one can note the circumpilar, saucer-shaped yellow disk, called the scutulum; and, finally, if one will scrape away this scutulum or any other adherent scales, one will find a raw, bleeding surface. Fortunately, this disease arises but seldom in the New England states. We see numerous instances of this infection in our hospital clinics, usually in the eastern European, almost always in the Russian Jew who has evaded the vigilance of the immigrant medical inspector. In this disease there is not only an alopecia (which is permanent) but also an insidious destruction of the skin and its adnexa, so that in the neglected and untreated cases the end-result is a thin, cigarette-paper-like scar tissue covering the skull, all else is gone.

In these two diseases, ringworm and favus, the hesitating observer may clinch his doubtful diagnosis by a microscopic examination. Remove a hair or a scale from the affected area, but choose the hair in preference if a diseased hair can be found. Place this material on a slide and pour several drops of ether upon it to remove the confusing fat drops. Add KOH in 40 per cent. strength to dissolve the keratin and render the object more translucent. Apply the cover-glass and examine under a high, dry lens with the transmitted light largely excluded. The typical mycelium and spores reveal the true nature of the process.

To return a moment to the effects of systemic toxemias on the scalp. With two notable exceptions the lost hairs are so evenly distributed that we never note any sense of bald areas; one hair in every twenty, one hair in every ten or less, disappears and we observe a slight or marked general thinning of the hair, nothing more. As a rule, severe alopecia, subsequent to infectious diseases, is fortunately rare and the chances of return are generally most favorable. The two prominent exceptions to the above rule of thinning are in syphilis and in alopecia areata.

In syphilis we meet this focal loss of hair, and we look for it first of all above the ears, and from these two points this phenomenon extends gradually backward and upward, and if the dis-

ease continues untreated or unchecked the process involves the whole scalp even to complete baldness, but such a contingency is exceedingly rare; and let me state in passing that syphilitic alopecia is by far the exception and not the rule, contrary to popular belief. There is a probable reason for this focal alopecia in syphilis. In most of our infectious diseases we are dealing with a general, one might say distant, and not localized toxemia; in syphilis, on the other hand, we have, to be sure, the usual general poisoning of the infectious process, but we have also the focal toxemia. The spirochetes of early syphilis are borne by the blood-vessels probably to all parts of the body, and therefore to the scalp. We know from our knowledge of anatomy that the finer arteries of the skin project at regular intervals vertically upward to the free surface like the trunks of a tree, and then, like its branches, spread out on the surface in the form of capillaries in a circular arrangement. Such a structural arrangement would seem to explain the localized, more or less circular depilating action of the syphilis virus and its toxins.

In *alopecia areata* we have a second type of definitely localized baldness. Here one must hesitate in stating too explicitly that the cause of this disease is a toxin. At least ten years ago Jacquet, of Paris, drew our attention to the frequent concomitance of ulcerating teeth and alopecia areata and he must have been one of the first medical men to suggest the rôle of focal pus as a cause for distant, subsequent, pathologic processes. Be that as it may, one must today appreciate the fact that many individuals affected with this form of patchy loss of hair are likewise suffering from abscesses in their teeth. On the other hand, careful observers have noted too frequently in these patients the history of nervous shock to be able to ignore the fact that such a factor may play an etiologic rôle in at least certain of our cases.

The diagnosis of alopecia areata is a very easy one. Suddenly or gradually the victim notices a single bald area on the scalp or in the beard. Slowly or rapidly, as the case may be, this area increases in size and simultaneously one or more similar

patches may develop. This is all, and the now worried patient comes to us and we note the patchy loss of hair. The diagnostic feature of the case is that there is no redness of the scalp, no scaliness, no infiltration, no papulation, no subjective symptoms —just one or more, single or multiple, discrete or coalescent, round or oval, small or large, totally bald areas. But let us look once more before stating finally or too categorically that the patch is totally bald, for around the periphery we may note one or more peculiarly formed hairs of larger diameter distally than proximally, the so-called pathognomonic exclamation-point hair. The disease with or without the best of care may progress locally until total baldness of the scalp and beard may result; the eyebrows and eyelashes may share in the general defluvium; and in the end the patient may stand before us a hairless being. Such a fate bodes ill for the future, but experience has led us to believe that if eyebrows and lashes persist the patient will eventually regain his normal appearance.

The *loss of hair from exposure to x-rays* is naturally a phenomenon relatively new in our experience, but it is a condition which we as practitioners must appreciate and recognize and a contingency which the radiologists must always bear in mind and guard against. Nowadays not many weeks elapse in which the busy dermatologist is not confronted with this new entity, and he must not make mistakes, for this condition is increasing in frequency almost *pari passu* with the ever-widening scope of *x*-ray investigations. Approximately ten days after the improperly or insufficiently screened exposure the hair begins to fall and continues to fall in proportion to the susceptibility of the patient and to the length or the frequency of the exposures up to a maximum total loss. In the still more severe cases there may be not only alopecia but also erythema and even vesiculation, but these conditions are now, fortunately, growing to be less commonly observed. One may well ask how to differentiate this type of alopecia from other forms, and especially from that of alopecia areata. The loss of hair following *x*-radiation is apt to be of somewhat large extent, it is apt to be definitely on one or both sides of the head or directly anterior or unquestionably posterior,

unless, of course, this loss of hair was intentional, for at the present moment skilled dermatologists are making use of this depilating power of the rays to produce the fall of hair in cases of ringworm and favus, thus depriving these plants of their principal food supply and consequently causing their rapid death and disappearance. In such circumstances the loss of hair is patchy. In both of these contingencies, however, the suspicious observer could make the proper inquiries, learn the truth, and clear up the mystery. We must also be on our guard about confusing *x*-ray alopecia with that due to syphilis. Last year a physician consulted me on account of a marked loss of hair over the occipital region. He said with some heat that he was ashamed and exasperated by the furtive looks with which some of his colleagues regarded his head and with the open tauntings of others who asked him where he "got caught." To one familiar with the exact nature of syphilitic alopecia such suspicions and accusations would have been impossible, but as yet the knowledge of *x*-ray alopecia has not filtered down to all members of the medical profession, and, of course, has not come to the ear of the laity to any great extent. The truth in the case of this unfortunate physician was easily obtained—the man had had a chronic headache and repeated colds and the "throat and nose" specialist had requested and obtained radiographs of the man's frontal sinus, the exposures being made anteriorly and posteriorly.

Fortunately, in *x*-ray alopecia the prognosis is almost always good, but some of the victims frighten us a good deal because their recovery is sometimes delayed for months. Proper treatment hastens perceptibly the regrowth of hair and should always be employed.

We come now, gentlemen, to the crux of this lecture—the loss of hair due to the admixture of heredity and infection, the so-called *alopecia prematura seu alopecia furfuracea.*

When a young person comes to consult you for loss of hair of the type now under consideration you will almost always glean two facts—*i. e.*, a present or a past dandruff and the story that the father, or the older brother, or the grandfather lost

his hair early; less frequently that the mother or the grandmother suffered the same fate—in other words, it is much more often the male who is attacked and who in his turn propagates the disease than the female. Thus I personally consider heredity the principal cause of alopecia furfuracea; in other words, the future victim is born with a lack of immunity to the bacterium of seborrhea and whether he acquires the infection or subsequently produces an immunity to it depends upon the conduct of his life and the treatment of his scalp. It is the conduct of his life in this respect and the care of the scalp which have prompted me principally to present this thesis on premature baldness and which we will now discuss.

Hygiene of the Hair.—A healthy body militates against future dandruff. Plenty of sleep, simple food eaten slowly, abundant daily and not too violent exercise in the open air, daily bathing, but not of the scalp, good morals, and avoidance of excitement should be our aim, for our statistics show that the young men and women who lead nerve-racking, sedentary lives combined with too rich and too abundant food and drink are the all too common sufferers from this affection. The hygiene of the scalp throughout early life means much to its future welfare, and there can be no doubt that the prevailing ignorance of the care of the hair must be fought by a campaign of education if we want to restore to civilization the full heads of hair which the savage still enjoys.

Let us begin with the child. There is no hard-and-fast rule as to the exact frequency with which a scalp should be cleaned. As soon as an abnormal amount of grease presents itself the hair should be washed. This maxim should obtain throughout our lives. In early childhood the average scalp should be shampooed once a week because we know how rapid metabolism is at this period of life.

Adolescents should wash their heads once in two weeks as a good average. After the age of puberty we should all shampoo once in three or four weeks according to the dryness or greasiness of our scalps. As to the choice of soaps we must be guided by circumstances—a greasy scalp requires a drying soap, such

as castile or ivory or possibly tar; a normal scalp is best served by any good so-called toilet soap; a dry scalp is best washed with a superfatted soap. It is, therefore, evident that the increasing practice of the daily sousing of the head in shower-baths and in ocean or fresh water bathing is a custom to be severely condemned. Our scalps and hair are normally oiled by a special fat secreted by our sebaceous glands, and any constant artificial removal of this normal fat must of reason prejudice the well-being of our hair.

The question of our head coverings must be taken into consideration. A moment's thought will reveal the fact that those races which have never worn hats are today spared the humiliation of baldness, and so our false prophets have cried that if we don't want to lose our hair we must follow their example and go hatless; but these men forget the dangers of too great cold and too great heat to men whose ancestors have for generations protected their hair and their brains from the extremes of our so-called temperate climate. It can be safely argued, I believe, that our modern fashion of trimming the hair short does not afford men, at least, sufficient protection against the winter's cold or the summer's heat. Then, too, we must remember that the African negro and the American Indian, our models in this respect, are provided with dark and greasy skins and black and oily hair, conditions which protect them from the dangers of the summer sun. But there is a lesson to be learned from these facts, nevertheless, and a wise compromise to be made. Let us, therefore, counsel a warm, loose head covering in the cold months of the year, no headgear in the really temperate periods, and a flexible, easy, light straw hat during the hot months when we are actually in the direct rays of the sun, and this is especially true when on the bathing beach, for the drops of water on our hairs act as individual burning glasses. There is also one exception to these temperate and warm weather rules. Always insist on a hat at all times when motoring—the dust of a road is dirt, dirt which may contain sputum, feces, and urine, dirt which it would seem wise to keep out of our head. Finally, let us most emphatically advise against the prevailing

custom of wearing hats in the house, in the office, in the club, and on long hot railway journeys.

From the beginning the selection and care of hair-brushes and combs should receive attention in our almost inevitable struggle against scalp infection. Girls and women do not need brushes and should never use them. Fashion decrees that the hair of men must lie flat, and thus brushes for them become a necessary evil, but let them choose the softest brushes compatible with this unwritten law. We all require combs. Let them have long, blunt teeth placed far apart, and avoid those of porous material. Never sanction the use of combs or brushes to remove dandruff or dirt, for this maneuver merely adds fuel to the flames—trying thus to remove the products of infection we merely infect the scalp still further. Combs and brushes must be kept as aseptic as possible and we must recommend strongly as a minimum a bi-weekly soap-suds bath with subsequent immersion in alcohol and a final exposure to the sun for several hours. Combs or brushes should never be lent or borrowed, and an individual's own utensils should always be taken to the barber or the hair dresser and subsequently treated as described above. It is a curious law that prohibits public combs and brushes in hotels and sleeping cars and allows them in those hot-beds of infection which we call barber shops and hair-dressing parlors. The use of side combs is an unnecessary evil and should be discouraged. Hairpins should be boiled frequently.

Barber shops are a necessary part of civilization, but we physicians must in future exert our influence toward their more hygienic management. Regular customers should be obliged to bring their own combs, hair-brushes, and shaving brushes; and the present custom of storing at the shop their individual implements should be abandoned, for the dust of such an environment is impregnated with other men's diseases; changes and substitutions can occur and there can be no certainty that these necessary articles are ever cleaned and protected from subsequent contamination.

Freshly sterilized combs and brushes should be supplied to transient patrons at an increased cost, of necessity, and razors

and scissors and especially clipping machines, also freshly sterilized, should be provided for every customer. It should no longer be possible that a barber should treat a fresh customer without washing his hands, that he should drop a utensil on his thoroughly infected floor and apply it without further ado to a man's head, that he should take from the used towel receptacle a dirty towel to wipe the dust from a man's brush, that he should wet with his saliva a finger to test the sharpness of a man's razor. These, gentlemen, are no exaggerations, but practices which have been observed personally in some of the best barber shops in America.

From what has been said it is evident that much must be done to counteract the fate that lies in wait for the individual who has inherited no immunity to the organism of seborrhea. When this bacterium has gained an entrance to a favorable soil, dandruff results, and, if left uncured or untreated, loss of hair ensues sooner or later in the great majority of instances.

The **diagnosis of seborrhea** or of its sequela, alopecia furfuracea, requires no great skill. The scurfy scalp, the dandruff on the coat collar, the itchy head, the reddened skin, the dry or greasy hair, the retreating forehead, the gradually developing tonsure, the insidious general thinning of the hair, are all, alas, too frequent pictures all about us and need no further consideration here.

Treatment of Alopecia.—And now, gentlemen, we have described the different varieties and types of premature baldness. What can we do to cure or relieve them? Before telling you what seem to be the best modern applications let me ask you to rehearse in your minds the contributing factors as they have been described and enumerated, and then do you, in your turn, apply them to each individual condition. These factors should perhaps be your main guides toward treatment, for without such prophylactic injunctions your care of the case would be futile.

Ointment A.

℞. Sodii biborat. 25
Ceræ albæ } āā 3 5
Sulph. præcip. }
Aq. rosæ. 8
Ol. petrolat. 20

S. Sulphur cream.

For the first month this ointment should be applied in the least possible amount directly to the scalp one night a week; for the second month one night in ten days; for the third month one night in two weeks; and subsequently the day the hair has been cut or as soon as grease collects on the skin or the hair. On the mornings following the applications of the ointment the scalp should be shampooed with an appropriate soap (*vide supra*).

Three mornings a week (never at night) one of the following washes should be rubbed gently on the scalp:

Wash A. (If there is dandruff.)

℞. Hydrarg. chlorid. corrosiv. 25
Euresol (pro capillis) 8
Sp. formicarum 30
Ol. ricini 0–10
Alcohol ad. 250

Or Wash B.

℞. Acid. tartaric. } āā 2
Chloral hydrat. }
Ol. ricini 0–8
Alcohol ad. 200

Or Wash C. (If there is no dandruff.)

℞. Pilocarpin. nitrat. 0·65
Quinin. sulph. 6·5
Tr. canthar. } āā 12
Tr. capsic. }
Alcohol ad. 250

Or Wash D. (If the hair is oily.)

℞. Hydrarg. chlorid. corrosiv. 2·5
Aq. ammoniæ 4
Sp. æther. } āā 25
Sp. lavandul. }
Alcohol ad. 250

Syphilis.—In this specific instance of infection the best results are obtained, of course, from appropriate internal treatment with salvarsan and mercury in combination, but the local disinfection and stimulation of Ointment A and Wash A will perceptibly hasten the return of the hair and free the patient from the patent, tell-tale evidence of his shame.

Ringworm and Favus.—There is only one good modern treatment for these localized infections, and that is depilation by means of the *x*-rays, but this maneuver requires the coöperation of a trustworthy, competent, skilful radiologist. There must

be no dangerous overexposures, for relatively harmless diseases must not be complicated by disastrous sequelæ. Let me ask you not to apply ointments to the affected areas five days before a contemplated *x*-ray exposure or for a space of ten days subsequently, because grease alters the susceptibility of the skin to the rays, and if, by mischance, a resultant dermatitis actinica is developing fats invariably render the exposed skin more vulnerable. Two weeks after the exposure we should apply night and morning the following:

Ointment B.

℞. Beta-naphthol..... 2
Sulph. flor.
Acid. carbol. } āā 4
Vaselin..... 32

This antiseptic, stimulating salve rather rapidly destroys the remaining epidermic infection (for *x*-rays are not parasiticidal but merely depilating), and also tends to hasten the regrowth of the new hairs.

Alopecia Areata.—In this disease our local indications are to destroy the microbacillus, which is present in such pure quantities in the so-called peladic utricle, and to encourage the new growth of hair, and therefore apply to the bald areas every night and to the whole scalp once a week Ointment A or perhaps better still:

Ointment C.

℞. Ol. cadin.
Acid. salicyl. } āā 2
Sulph. præcip.
Vaselin..... 32

These ointments must be thoroughly washed from the scalp on the following morning by means of castile soap and subsequent swabbing with alcohol. Then apply with great caution

Wash E.

℞. Ol. tiglii..... 1–3
Ol. terebinth..... 48

diluting this wash at first with alcohol if papules, vesicopustules, or soreness develop.

x-Ray Alopecia.—After the regulation two weeks' interval the scalp can be stimulated very properly and efficaciously with Ointment A and Washes A or B.

Alopecia Furfuracea.—The treatment of this common affliction is the same as that recommended under the heading of general infectious diseases. Remember all the prophylactic measures described and enumerated above and take care to warn your patients that this is a long and tedious process—in fact, that it must be pursued diligently and faithfully for years to come. Remind them that dentists have educated them to take perpetual care of the teeth by daily brushing and frequent dental examinations, and make them appreciate the fact that hair and teeth are formed of essentially the same substance, and that both are liable to the deteriorating influences of modern civilization. By such advice only, it seems to me, can we encourage our patients to follow this long and arduous path of duty. Let us be guided by the principle that baldness is not a necessary evil, and that by incessant and therapeutic care it can be made to disappear from our sight.

Finally, in all these various types of alopecia skilful massage is of great service, but never let it be employed when visible signs of inflammation are present, and among these signs dandruff is to be especially included.

This, gentlemen, completes this presentation of this practical question which affects sooner or later so many members of our community. It is not a trifling subject, and any man who has witnessed the unhappiness and mortification of the many victims of alopecia will bear testimony to the truth of this assertion.

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ECZEMA IN CHILDHOOD

Clinical Manifestations; Objective Symptoms; Etiology; Management and Treatment; Necessity of Investigating Each Case Carefully and Outlining the Treatment According to the Etiology.

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THE earlier teachings concerning eczema and childhood were confined to the skin alone, because the knowledge at the time was limited to what could be seen by the naked eye and under the microscope. Eczema, therefore, belonged in the domain of dermatology, and the emphasis of treatment was laid on external applications to the skin. Although in some instances such applications were quite satisfactory, and apparently cured the eczema, there still remained a large group of cases which only showed slight or no improvement. Investigators, therefore, commenced to look elsewhere for a cause which might be back of the skin manifestation. It was then found that the digestion played a very important part in the cause of eczema and, therefore, the service of the pediatrist was necessary to regulate the diet of the child. As time went on, the relative importance of the two specialties became reversed, so that at present it is fair to say that eczema in childhood is a disease which falls primarily into the domain of the pediatrist, later going to the dermatologist, when necessary, for local treatment. Sufficient knowledge of metabolism, digestion, and dietetics in infancy and childhood can only be attained by those who make a special study of the diseases of children, and the knowledge of facts necessary for a com-

plete understanding of the processes of digestion is attained only after many months of study and experience, while the number of external applications which are of any real value in the treatment of eczema in infancy or childhood are so few that they can be learned in a short time. If one specialty is to be consulted, that which can do the most should be selected. Eczema in infancy and childhood, therefore, is best placed in the specialty of pediatrics.

The following summary and case reports undertake to cover briefly the essential points known about eczema in infancy and childhood, and tend to show the relation of the older assumption of its external origin, to the more recent facts brought to light concerning its internal origin.

Clinical Manifestations.—Eczema in infancy and childhood does not show so many varied types as in the adult. The commonest symptom is itching, which is present in the great majority of cases, although occasionally it may be entirely absent. It may be coincident with or preceded by a skin eruption. As a rule, the itching is not constant, its appearance being associated with digestive symptoms. Usually disappearance of itching precedes an improvement in the skin. This irritation is present to such a degree in the eczemas of infants and children that even when the child is pinned down to the bed in such a manner that it cannot scratch, I have seen it wriggle into inconceivable positions in order to obtain friction of the affected parts. Gentle friction with the hand will often quiet an infant who is trying desperately to scratch itself. The scratch-marks leave raw, oozing, bleeding patches, which are easily infected, and may result in an impetigenous eczema. A nervous irritability is also a common symptom, which has led some of the German School to attribute eczema to a "neuropathic diathesis." This nervousness, in my opinion, is a secondary symptom rather than a primary cause.

Objective Symptoms.—In infants and young children the commonest form of eczema is seen especially on the face, cheeks, scalp, and back of the ears, and is called by Marfan and Feer the oozing, crusted eczema, in contradistinction to the disseminated, dry eczema. This type of eczema usually commences on the

cheeks, with the formation of small red papules, which coalesce, and, if rubbed, become red and oozing. The secretion dries in thick crusts, and when scratched bleeds easily. The skin, in these cases, is usually thickened, and the lymph-nodes are always enlarged in the neighborhood of the affected areas. The general health later becomes impaired if the eczema persists any length of time. This, however, is probably not due to the skin eruption, but to the condition underlying it. In some instances the eczema alternates with attacks of asthma and bronchitis. Patients suffering from eczema are likely to have periods of diarrhea associated with improvement of the skin. Earlier observers have laid much stress upon these coincidences, and believed that it was not good to "drive an eczema in." An example of this is shown in the case of a boy of ten years who came to me because of asthma. His history showed that he had had a severe general eczema, which external treatment did not affect, until he was thirteen months old, at which time a new ointment was applied to the skin and resulted in immediate improvement. Coincident with the disappearance of the eczema he had his first attack of asthma. It might be assumed that the eczema was driven in, with the resulting asthma as a consequence, but there is sufficient evidence to prove that some types of eczema and asthma are the same disease, with symptoms in different parts of the body. In the majority of asthmatic cases there is a history of an early eczema, but the fact that a child has eczema does not necessarily mean that later it will have asthma. Conversely, a few cases of eczema are followed by asthma or an idiosyncrasy to some food.

The crusted form of eczema very often stops at the beginning of the second year, when there is a reduction in the quantity of milk an infant takes in the day, and other foods are added to the diet. It is a curious coincidence that the eruption of teeth is very frequently associated with an exacerbation of eczema. In nearly all these cases, when the teeth are coming through, the eczema, which may have entirely disappeared, returns until the teeth are through the gums. It should, therefore, be borne in mind that even when the diet has been properly regulated, erupting teeth may cause a relapse in the skin condition.

A second type of eczema, which is seen in late infancy and childhood, is the dry, disseminated, scaling form. This is the most chronic form, and the earliest lesions to appear are so similar to certain forms of urticaria that it is often impossible to distinguish between the two. As time goes on the urticarial-like eruption becomes a typical eczema. This sequence of events can be produced experimentally or accidentally by giving too much egg to an individual who has an idiosyncrasy to hen's egg. There is little doubt in my mind that this form of eczema is usually a late stage of urticaria. The general glandular enlargement, seen in these cases, is often associated with an enlarged thymus. This might be taken as an explanation of the sudden death which occurs occasionally in eczema, and which pathologic section designates as status lymphaticus.

A study of the differential count of the blood in eczema, asthma, afebrile chronic bronchitis, and urticaria shows an increased number of eosinophils in the blood, often as high as 10 per cent.

Etiology.—The diversity of opinion as to the causes of eczema is due to the fact that the means used in studying the cases were not sufficiently accurate to demonstrate any factor of etiologic significance. More recently it has been possible to differentiate the various types of the disease by microscopic examinations of the stools, or by the skin tests with foreign proteins.

The commonest exciting external causes of facial eczema in children with a delicate skin are cold, dry winds, which alter the physical composition of the exposed parts, and the use of hard water or strong soaps, lack of cleanliness in the folds of the skin, irritating discharges from the nose or ears, and acid, burning stools. Infants' and children's skin is more delicate and more easily harmed than an adult's. There are certain skins that are peculiarly susceptible to different forms of external irritation.

Case 1.—C. O., girl of five months, is an example of the simplest form of eczema due to external irritation. She was breast fed, and at three weeks eczema broke out on the face and spread until both cheeks were rough, red, and oozing serum. This eruption appeared on the first raw, windy day this winter and

became progressively worse, especially when the face was washed with soap. The use of soap was stopped, and a simple zinc oxid ointment was applied. In all probability the eczema will then clear up if the child is kept out of the cold, sharp winds.

The treatment of eczema from internal causes is a different problem, as it is much more difficult to find a definite etiologic basis in these cases. Sometimes, however, by a careful study of the diet, and the sequence of events, enough evidence may be accumulated so that it is possible to determine the causative agent. A common cause is usually found to be overfeeding, and according to the figures of More and Kolb over half of the children with eczema are overfed, only 26 per cent. being undernourished. In my experience the physical development of the patients would seem to substantiate these findings. but a closer study of their diets show that overfeeding alone is not the sole cause in a large majority of these cases of eczema. The commonest food component to cause eczema, when given in excess, is fat. A typical example of this is shown by the following case:

Case 2.—E. P., a boy of six months, has an oozing eczema of the face of two months' duration, which presents the typical text-book picture. He was entirely bottle fed, had no symptoms of indigestion, but was slightly constipated. He was on a formula of fat 4.5 per cent., lactose 6 per cent., and protein 1.5 per cent., 7 ounces every three hours, six feedings. He was gaining regularly, and, aside from the eczema, acting well. The scratch-marks on his face and the way he rubbed his head on the pillow showed that itching was a prominent and distressing symptom. The mother says that when he first came to the clinic it was so bad that he slept very little at night and was very irritable. The first examination of the stool, two weeks ago, was as follows: Grayish yellow, smooth, a little dry, and crumbly. Under the microscope it showed a large excess of fat in the form of soaps. (The technic employed in the microscopic examination was that described in the Boston Medical and Surgical Journal, 1910, clxii, page 134). Since he was receiving more fat in his food than is usually considered wise, and since there was an

excess of fat in the stools, the amount was reduced to 2 per cent. The mother reported later that the eczema immediately commenced to improve. Today's stool examination showed only a slight excess of fat. We purpose, therefore, to reduce the amount of fat to 1.75 per cent., and to increase the amount of protein to satisfy the baby's hunger as well as to give him enough calories to grow, and expect that when he next reports the itching will have stopped entirely, and there will be further improvement in the skin.

This type of case is so common in infancy that many practitioners reduce the amount of fat in the food in all cases without examining the stools. In most cases this procedure would be justified by the clinical improvement which is likely to follow, but there is a small percentage of cases in my experience which do not show any fat in the stools, and in such instances a reduction of the fat would unnecessarily take away a desirable food. It is safer, therefore, to always examine the stools under the microscope, even in cases which seem to be complete without such an examination. In this connection it is wise to bear in mind that the power of digesting fat varies in different individuals, and that amounts which would be normal for one would be an excess for another. The fact, however, that there is only a small amount of fat in the food does not mean that the fat has no connection with the eczema.

It is difficult to explain why fat is not tolerated and absorbed well by most eczematous children. There must be some abnormality in the absorption or in the internal metabolism of the fats. Up to date, however, science has offered us no suitable explanation for a well-established clinical fact. External applications in this type of case are, of course, of considerable value in controlling the itching and allaying the irritation, but in the majority of instances they play a lesser part in the complete cure than does the diet.

Eczema may also be associated with an excess of starch in the stools, and although this is not a common finding, its reduction in the diet usually results in an improvement in the skin. If there are signs of indigestion, these symptoms im-

prove with the eczema. Since all starch contains some protein, even though in small amounts, it is not possible to say definitely whether the starch or the protein in the starch is at fault.

Before considering the rôle of protein in eczema it is necessary first to speak briefly of the salts in the food. The Finkelstein School reports cures of infantile eczema by giving a food poor in salts. My experience with this method is so slight, and the knowledge of the part the salts play in the metabolism so small, that I will not venture to judge this method of treatment. It is possible that there is some connection between an excess of salts in the food and too much fat in the stools.

The rôle played by protein in eczema cannot be demonstrated by an examination of the stools. There are many facts, however, which lead investigators to consider eczema a symptom of anaphylaxis to a foreign protein. The earliest suggestion of this was made by Czerny who described the clinical entity "exudative diathesis," in which he includes eczema and asthma. It fits in, however, so nicely with sensitization to foreign proteins that it is probable that most of its symptoms are manifestations of anaphylaxis.

The next group of cases are examples of eczema primarily due to special foods. This group deals with sensitization to foreign proteins or anaphylaxis. Examination of the stools is of no value in determining the cause of this type of eczema other than showing to what an extent a fat indigestion complicates the picture. As a rule, a large proportion of these cases have too much fat in the stools, but in my experience this is only of secondary importance in the dietetic treatment of the disease. External irritation also plays a secondary part in this group of cases, which are said to be due to anaphylaxis. The following 2 cases are examples of the anaphylactic type of eczema:

Case 3.—E. B., girl five years old, has had eczema all her life and had received all kinds of external treatment, without improvement. Her eczema could be described as a general, discrete, papular eczema, scattered over the entire body. Other-

wise the physical examination was normal. Skin tests were done for various foods, according to the method described by Schloss (American Journal of the Diseases of Children, 1912, vol. 3, page 341), and positive reactions were obtained to hens' eggs and cows' milk. Negative reactions resulted from the other proteins tried. Egg was, therefore, entirely omitted from the diet, and the milk boiled and reduced in amount from a quart to a pint a day. The diet, otherwise, was unchanged, and within five days the eczema had entirely disappeared. Two weeks later, during which time she had been free from eczema, a hard-boiled egg was given, and within eighteen hours an urticarial-like eruption appeared on the skin, which the mother said resembled the onset of the previous eruptions, which later turned into eczema. Since then egg has been entirely omitted from the diet, and as a result the skin has been perfectly normal.

CASE 4.—G. D., girl, seventeen months old, was weaned at four months and given a formula of modified milk which was followed shortly by a scattered, papular, scaling eczema over the back of the neck and trunk. Otherwise her physical examination was normal. Skin tests for the following proteins were done: hen's egg, which resulted in a very large reaction, cows' milk, a moderate reaction, and rice, a slight reaction. (The methods of preparation of the vegetable proteins are described in the Boston Medical and Surgical Journal of March 29, 1917, and July 19th, 1917.) A microscopic examination of the stools showed a very small amount of fat. On the basis of these findings egg and rice were omitted from the diet and the milk was boiled. One month later the parents report that the eczema had almost entirely disappeared. In the interval rice was given once, and resulted in a fresh eruption on the skin. The offending articles of food in this case were primarily egg and rice, and secondarily milk.

Some time ago while desensitizing a child that was sensitive to eggs, I found that if too much egg was given to the patient there resulted an eczematous eruption on the skin, which disappeared on reducing the dosage. Schloss had previously made the same observation, and has reported, in discussions, results

of his investigations. Blackfan, at about the same time, studied sensitization to foreign proteins by means of the skin test. The connection between asthma, eczema, chronic afebrile bronchitis, and urticaria has long been suspected. The point in common in all of these diseases is an increased number of eosinophil cells in the blood, 6 per cent. is quite usual, and 12 per cent. not uncommon. Schloss has shown that if a foreign protein is injected into small animals, there is an increase in the number of eosinophils in the blood on the eighth to the twelfth day following the injection at about the time sensitization was commencing. This leads one to assume that there is some relation between the two phenomena. If it is true that eosinophil cells are an index of sensitization, then anaphylaxis must play a part in all cases showing an eosinophilia. When an infant is given cows' milk for the first time the blood shows an increased number of eosinophils between the eighth and twelfth days, after which the differential count becomes normal again as the baby "becomes used to the milk." Evidence other than the frequent positive skin tests to foreign proteins, the clinical sequence of events, and an eosinophilia is lacking to establish an anaphylactic cause for eczema, but the fact that eczema will disappear from the skin of a child giving a positive skin test to egg when the egg is removed from the diet, and will return again when egg is given, is prima facie evidence that the egg is the cause of the eczema in this case.

The question is often raised as to how specific the skin test is, and whether a positive test may not be obtained in healthy individuals. In answer to this I may say that a routine skin test for egg-white was made on 100 unselected infants and children entering the Children's Ward at the Massachusetts General Hospital, and only one positve reaction was obtained, and in this case there was a slight eczema. Blackfan found only one patient which showed any evidence of susceptibility to protein by cutaneous or intracutaneous tests.

The following table gives the results of positive skin tests in eczemas:

Protein.	Blackfan,[1] 21 cases.	Schloss,[2] 43 cases.	Talbot, 16 cases.
Egg-white	21	14	14
Cow casein	17	12	4
Human milk	10	3	
Barley	8		0
Horse-serum	7		2
Meat extract	6		3
Rice			5
Oats			3
Orange			1
Corn			1
Fish			1

Many cases of eczema react to more than one protein, and it is often difficult to determine what particular protein is causing the most trouble. When a positive skin test is obtained, it is best, except in rare cases, to remove the offending protein from the diet, after which the skin eruption almost invariably disappears. Unfortunately, however, some cases do not give any positive skin tests. I have in mind one particular case in which sixty different proteins were tested without any positive tests. Very often, also, a positive skin test is of no value in the treatment of eczema, as, for example, in the case of the child who reacted to corn pollen, but gave negative reactions to the food proteins. It is obvious that the corn pollen could not be the cause of the eczema.

In *treating cases of eczema due to anaphylaxis* two classes must be considered. The baby on human milk is an example of one type of case:

Case 5.—R. T. H., girl, three weeks old, entirely breast fed and gaining normally, when a fine papular rash appeared on the cheeks and body. A careful study of the mother's diet revealed the fact that previous to the appearance of the eruption on the baby's skin the mother had eaten about a pound of chocolate candy. Chocolate was, therefore, omitted from the diet, with the result that the baby's eczema immediately disappeared. After two weeks' time chocolate in the form of cocoa was taken,

[1] Blackfan: Amer. Jour. Dis. Chil., 1916, xi, p. 441.

[2] Transactions of the American Pediatric Society, 1915, p. 60.

and within twenty-four hours the same papular rash again appeared over the baby's face and neck. Chocolate in all forms was, therefore, entirely omitted from the mother's diet, and since then the baby has showed no signs of further eruption. This case was easily handled after it was found that chocolate in the mother's diet was the cause of the eczema.

Another type of case in this class gives a positive skin reaction to either human or cows' milk, or both, and by omitting the milk from the diet becomes entirely well in about five days, only to have the eczema return again after a few days, without any explanation. It is a difficult problem to feed a baby on a food which does not contain milk in any form, and since such a procedure is not without risk to the baby, I have, therefore, stopped using it, particularly since improvement is not permanent.

The second class of cases in the anaphylactic group is seen in children of twelve or more months of age whose diet contains other foods than milk. Treatment of this class of cases is easier because there are a variety of foods which may be given to the child. If a positive reaction is obtained to the protein of rice in this group, as has happened in 5 of my cases, rice may be entirely omitted from the diet without any hardship to the child. Positive skin tests in older children with eczema are, therefore, of great value in planning the dietary treatment of the disease.

In the treatment of eczemas due to foreign proteins there are certain principles that may be applied. In the first place if a positive skin test is obtained, it probably is of etiologic significance, and, therefore, the protein to which the skin has reacted should be removed from the diet. Egg, which is the commonest offender, may be removed from the diet of a child of any age, whereas milk, which takes a larger and more important part in the dietary of the child, cannot be replaced by any other food. Laboratory experiments have shown, however, that when a foreign protein, as a specific example, we will take cows' milk, is heated to 240° F., a change takes place in the milk and it no longer causes an anaphylactic shock in a sensitized animal. Boiled milk acts in a similar way, but to a lesser degree. Therefore when milk cannot be excluded, it should be boiled. In a

few individuals that are sensitive to cows' milk small quantities of milk may be taken with impunity, while a large quantity causes indigestion. Under these circumstances it is wise to boil the milk and then give the largest quantity that can be taken without symptoms. Milk, furthermore, can be modified by inoculating it with a lactic-acid-forming bacteria. This affects the eczema favorably in some unknown manner. Subcutaneous inoculations of foreign protein may be employed to desensitize a patient. This procedure, however, is not free from danger, as it has been known to cause anaphylactic shock. In infancy, at least, it is better not to use subcutaneous inoculations, since they might result in death. As a substitute, desensitization by rectal injections of cows' milk may be used, enough milk being absorbed by the mucous membrane of the large intestine to desensitize the patient. In the case of other foods, such as rice, wheat, oats, and orange, etc., it is better to omit them entirely from the diet.

Summary.—The simplest form of eczema is that due to external irritation. As the disease becomes more complicated, we have added to this a lowered power for digesting fat, and on top of that, in the most complicated cases, a food sensitization. In order to demonstrate which of these three factors play the predominating rôle it is necessary to investigate each case carefully and outline the treatment according to the etiology.

CLINIC OF DR. HARRY A. BARNES

MASSACHUSETTS GENERAL HOSPITAL (NOSE AND THROAT DEPARTMENT)

VINCENT'S ANGINA

Differential Diagnosis; Is Vincent's Angina a Clinical Entity? Bacteriology; Etiology; Symptoms; Treatment.

December 1, 1917.

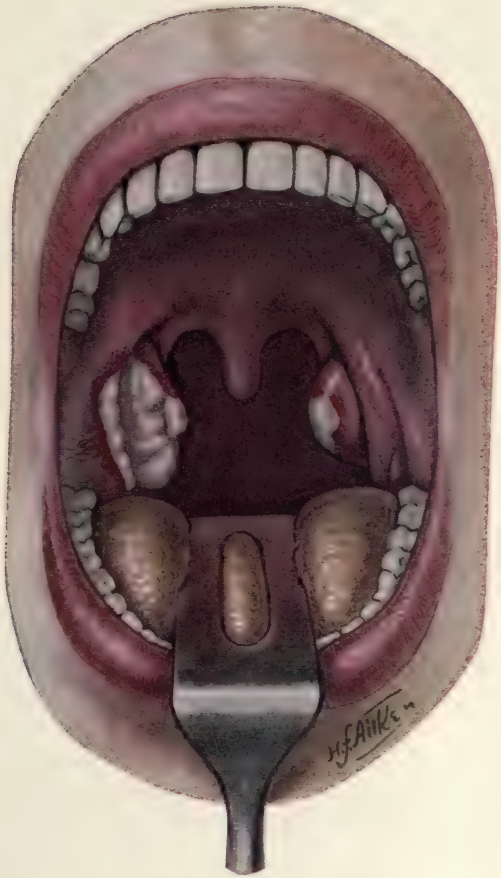
A. M., male, twenty-three years old, worker in a cotton mill, gives the following history: Ten days before coming to the hospital he awoke in the morning with a sore throat confined to the right side. There were no constitutional symptoms severe enough to make him remember them. The next day swallowing became very painful, and he consulted a local physician, who told him that he had an acute tonsillitis and advised an immediate tonsillectomy. The patient declined operation and kept at work, feeling somewhat under par, but having none of the general symptoms usually associated with acute infection. Swallowing has remained very painful and this discomfort is still confined to the right side. He has had occasional chilly sensations, but no actual chill. One week ago he noticed a slight swelling on the right side of the neck near the angle of the jaw, and this swelling has been somewhat tender to the touch for the past three days. He has never had a sore throat before and, with the exception of a gonorrhea two years ago, gives a negative venereal history.

Physical examination shows a man of medium size, well developed, but with a somewhat pinched and pasty look. Temperature 99.2° F.; pulse 78 and of good quality. The tonsillar gland on the right is enlarged to the size of a walnut, is freely movable, non-fluctuating, and tender on palpation. No other

glands are involved. On examination the jaw opens freely and there is no general swelling in the faucial region. The median raphé of the palate is in the central line. The tonsils are of moderate size and are fairly prominent beyond the faucial pillars. The right tonsil shows an ulceromembranous condition embracing all of its epithelial surface except a small area posteriorly near the supratonsillar fossa. The lesion extends anteriorly slightly over the border of the anterior pillar. Its edges are slightly uneven, though not ragged, and are slightly redder than the surrounding healthy tissue, but are not raised or everted. There is evidently considerable loss of tissue, as the surface of the ulceration is slightly concave, whereas the normal contour of the tonsil is convex. The tissues immediately surrounding the lesion are somewhat injected, especially at the base of the anterior pillar, where a network of fine capillaries may be seen. On the left tonsil is a similar lesion of much less extent and without any apparent loss of substance. The patient has not been aware of any trouble on that side. The breath is foul with an odor suggestive of Vincent's angina. (I may say here that odors arising from membranous and ulcerative lesions of the throat and mouth are by no means as distinctive as the odors of certain nasal lesions, such as syphilitic bony necrosis or atrophic rhinitis, which may often be diagnosed from smell alone. Nevertheless, information gained from them may be of great value even if we are obliged to admit that such evidence is often of an intuitive nature.) On wiping the surface of the lesions with a cotton-tipped applicator the membrane is found to be easily removed, very friable, and of a pultaceous, almost granular consistency, not unlike a thick paste of cigar ash. The exposed surface is uneven, slightly lobulated, and has numerous small bleeding granulations showing through the thin necrotic base. To the touch with the gloved finger there is no noticeable induration. The ulcerated surface on the right is extremely sensitive.

Differential Diagnosis.—We have here an ulceromembranous lesion of the fauces in which the diagnosis lies chiefly between diphtheria and Vincent's angina. Other affections, however, cannot be ignored, and we will consider them in inverse order

PLATE 2



VINCENT'S ANGINA

This illustration was made directly from the case reported in this clinic.

of the likelihood of their being the correct diagnosis in this case. For immediate diagnosis the microscope is our best aid. Two smears have been taken from the lesion on the right—one for examination with the dark field illumination; the other for ordinary microscopic examination after staining with carbol-fuchsin.

Acute Streptococcus Tonsillitis (*Septic Sore Throat*).—The duration of the disease, with only the mildest of constitutional disturbance, is sufficient to rule this out. During the first forty-eight hours I should think this might have been considered seriously. Cultures and smears would have corrected any error.

Syphilitic Ulceration (*Tertiary*).—The sudden onset, the glandular involvement on the right with tenderness on palpation, the character of the ulceration, and more particularly of the exudate or membrane, make this diagnosis extremely doubtful. Examination of the blood for a Wassermann reaction should be made if such a lesion fails to respond to ordinary methods of treatment.

Primary Syphilis (*Chancre*) *of the Tonsil.*—This affection is not so easily disposed of. The fact that the lesion in this case is bilateral certainly does not favor it. The character of the glandular enlargement does not suggest it. In chancre of the tonsil not only is the tonsillar gland enlarged (as it is in this case), but usually the whole group of upper cervical glands under the sternomastoid is involved, making a very pronounced swelling in which the outlines of the individual glands cannot be distinguished. However, this lesion is only ten days' old and sufficient time has not elapsed for the full development of a primary bubo. Also I may say that only last week a patient came into this clinic with a primary lesion of the right tonsil, proved both by the presence of undoubted secondary lesions and by the presence of the Spirochæta pallida in smears taken from the tonsil, in whom the tonsil gland alone was enlarged, and that only to the comparatively slight degree present in our case of today. There was, however, no tenderness on pressure over the gland as there is in this case. The character of the ulceration with its grayish granular exudate does not suggest chancre. Chancre of the tonsil may be simply an erosion with very slight if any loss of

substance; or there may be well-marked ulceration with a dirty yellowish exudate hardly membranous in character. In either case chancre of the tonsil usually is a pronouncedly indurated lesion, sometimes the whole tonsil apparently being involved. The acute pain favors a diagnosis other than chancre, though occasionally initial lesions of the tonsil give rise to a good deal of discomfort in swallowing. A Wassermann reaction probably would not help in this case, as the reaction usually does not appear till the fourth or fifth week after the appearance of the chancre. Our dark field examination will probably settle this point satisfactorily.

Diphtheria.—During the first few days of the disease this diagnosis could only have been disposed of by culture and examination of smears microscopically. The character of the exudate at the present time suggests Vincent's angina. When we add to this the absence of any marked general symptoms during a period of ten days the diagnosis becomes still more probable. Both the smears taken from this case show large numbers of the Bacillus fusiformis and its accompanying spirillum. The dark field illumination fails to show the presence of the Spirochæta pallida. Our tentative diagnosis, then, is Vincent's angina. The blood will be taken for a Wassermann test; also a culture will be taken from the throat to exclude any possibility of diphtheria. I never have seen a case, however, in which the organisms of Vincent's angina were found in very large numbers in the smears that later showed positive cultures of the Klebs-Löffler bacillus.

The **treatment** of this case consists in removing the exudate with cotton dipped in a 1 per cent. solution of cocain to lessen the sensitiveness of the ulcerations, and the application of a 5 per cent. solution of chromic acid. This is very mild medication, but a few daily applications are usualy sufficient to effect a complete cure.

December 3d. The patient's subjective symptoms have largely subsided. There is still slight soreness of the throat on the right side, but practically no tenderness on palpation of the enlarged tonsillar gland. The ulcerations on the tonsils are much cleaner,

the membranous exudate thinner, and the odor less pronounced. The extent of the surface involved has not materially changed. There is only slight sensitiveness when the membrane is removed with the cotton-tipped applicator. The temperature is normal. The patient looks brighter and his color is improved. Cultures taken two days ago for the Klebs-Löffler bacillus were negative. Local treatment with 5 per cent. chromic acid will be continued. For the general condition the tincture of nux vomica in the glycerophosphates of lime and soda is excellent.

December 5th. The patient has failed to return, probably because he considers it unnecessary. Unfortunately, we were to have taken his blood for a Wassermann this morning, and that phase of the case must remain incomplete. In view of the other laboratory findings, together with the clinical manifestations of the lesions and their very prompt response to the simplest treatment, the Wassermann reaction is of comparatively little importance in this particular case.

The foregoing case is a typical example of one of the forms of simple ulceration of the fauces, characterized by the formation of a membranous exudate in which large numbers of the Bacillus fusiformis and its accompanying spirillum are found, and in which no other specific cause for the lesion can be demonstrated. Such lesions are now grouped under the common name of Vincent's angina. They vary within tolerably wide limits in their appearance, but are always ulceromembranous in character, and usually conform to one of two general types—those simulating diphtheria and those having more nearly the characteristics of late secondary specific ulcerations. They are usually confined to the tonsils, but may extend to other parts of the fauces and pharynx, or may even be primary on these parts. Occasionally they occur on the mucosa of the cheeks or gums. I have seen 2 cases in which the region of the lingual tonsil was the only part involved. Cases have been reported as primary in the larynx, trachea, and bronchi.

Whether these lesions constitute a clinical entity or not is a question not yet fully decided, as the fusiform bacillus and its accompanying spirillum, though always present in the membrane,

cannot be proved to have any but a casual relationship to the lesions. Inoculation experiments have thus far given negative results. Some observers believe that the lesions are started by the streptococcus and that Vincent's organisms are secondary invaders. The mild character of the general symptoms in the average case, however, does not suggest a streptococcus origin; and there are good reasons for believing that Vincent's organisms, ordinarily harmless and saprophytic in character, and often found in essentially normal mouths, may, under certain conditions of lowered resistance on the part of the host, become pathogenic. The lesions are common in the poorly nourished or in those debilitated by general disease; and the most destructive and fatal forms of gangrenous necrosis in which these organisms are found often occur in subjects with leukemia or one of the other essential blood diseases. The fact that at times it seems to be mildly contagious, when several people in good health and living in close association are attacked successively, indicates a specific relation of the organisms to the lesions. This supposition has certainly not been weakened by the pronounced effect that the arsenomercurial preparations, so successful in the treatment of syphilis, have upon the disease. Certainly the lesions usually seen in the throat in which these organisms are found in preponderating numbers constitute a clinical picture distinctive enough to be considered an entity, and I think they are regarded as such by a consensus of present opinion.

Vincent's angina is an ulceration of the mucosa characterized by the formation of a necrotic membrane in which the Bacillus fusiformis and a spirillum are found in predominationg numbers. The lesions are usually confined to the tonsils, but no part of the upper respiratory and gastro-intestinal tract is exempt, though cases involving the larynx, trachea, and bronchi are rare. The ulceration is usually not deep, but it occasionally becomes so, and more or less of the whole tonsil may slough away; or it may spread to the surrounding tissues, and the faucial pillars, the palate, and the pharyngeal walls become the seat of a destructive gangrenous necrosis.

Bacteriology.—The Bacillus fusiformis as seen in smears

direct from the lesions is a double-pointed bacillus, somewhat swollen in the middle and often presenting a beaded or barred appearance due to a varying number of deeply stained granules in its protoplasm, which is elsewhere but lightly stained. It is non-motile and decolorizes by Gram. In anaërobic cultures its morphology is very variable. Some of its forms are sinuous

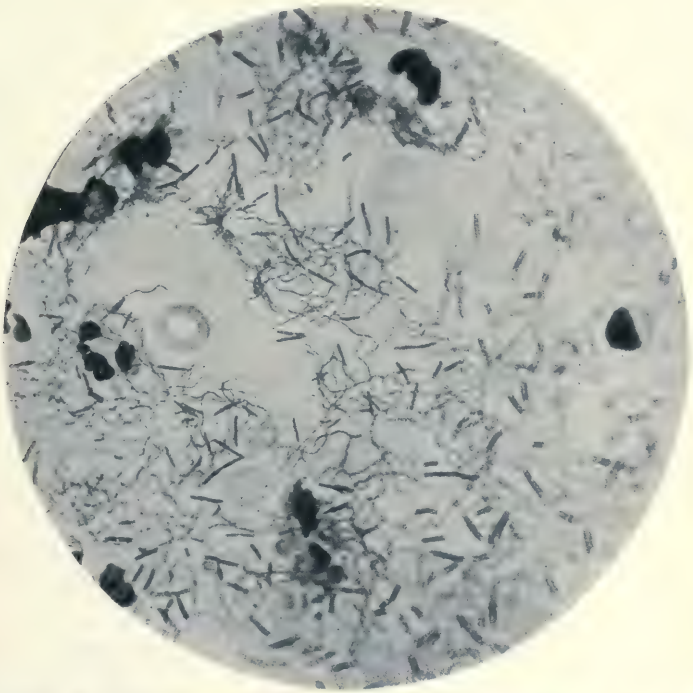


Fig. 105.—The organisms of Vincent's angina. At the periphery of the field the organisms are not in focus. (Barnes on the Tonsil.)

and when granules are absent simulate a loosely wound spirochete. The spirillum which always accompanies the bacillus is a corkscrew-like organism not unlike the Spirochæta pallida, but with fewer twists and wider spirals than the latter, and when seen under dark field illumination is more rapid in its rotary movement. Both organisms are anaërobic. They have been regarded by some observers as different developmental stages of

the same organism[1]; others consider them quite distinct and always growing in symbiosis.[2] They were first described by Miller in 1883 as occurring in normal mouths, but more especially in those of persons not addicted to the use of the tooth-brush. Their presence in the lesions of ulceromembranous angina was first reported by Rauchfus in 1893. Since then the organisms have been found in necrotic and suppurative processes of all sorts and in widely different parts of the body. Their association with the lesions of ulceromembranous angina was reported by Plaut[3] in 1894 and by Vincent[4] in 1896, and Vincent's subsequent work has given his name to the disease.

Etiology.—We assume that the above-described organisms are the direct cause of the disease. There are, however, certain predisposing causes that are of importance. Careless hygiene of the mouth is probably responsible for a large proportion of the cases of the less serious type. Combined with this, any of the causes of malnutrition make conditions favorable for the development of these lesions. Its more serious forms are usually secondary to other infections, such as diphtheria, scarlet fever, or measles. Patients with leukemia seem especially subject to the disease, and these cases usually terminate fatally. It is interesting to note that the disease is very common among the English and French troops in the trenches. Bouty[5] reports that it represented 23 per cent. of all the throat cases occurring in one of the large British military hospitals in France.

Symptoms.—The subjective symptoms are usually mild, as in the case here reported. The temperature is seldom raised beyond 99° F. and is often subnormal. Even the more severe and fatal cases are no exception to this rule. The breath is heavy and very offensive and often characteristic. Slight enlargement of the cervical or submaxillary glands is usual. The ulcerated surface is always exquisitely sensitive, and this soreness of the

[1] Tunnicliffe, Ruth: Jour. of Infec. Diseases, Vol. III, 1906, p. 148.

[2] Krumwiede, C., Jr., and Pratt, Josephine S.: Jour. of Infec. Diseases, Nov., 1913.

[3] Deutsche. med. Wochenschrift, 1894, xlix.

[4] Ann. de l'Inst. Pasteur, 1896, 488.

[5] British Med. Jour., Nov. 24, 1917, p. 685.

throat is the most marked subjective symptom. The membrane may be on one or both tonsils and is usually single. Sometimes it is multiple and discrete. When the ulceration is shallow and its edges not very sharply marked the lesion simulates diphtheria. When the edges are sharply defined the lesions present the punched-out appearance of the specific ulcerations. The membrane is usually ashy in color. It may be white, whitish gray, gray, grayish yellow, or even of a greenish tinge. It is very friable, pultaceous, and even granular, and is easily removed, leaving a granulating bleeding surface beneath. It quickly re-forms. The graver forms of the disease are fortunately rare. Large areas of the mouth and pharynx become involved and the necrosis extends deeply. The pulse is rapid and feeble and the prostration extreme. Glandular enlargement may be marked. Death usually results from exhaustion.

The diagnosis rests upon the finding of the specific organisms in smears taken from the lesions, and in the exclusion of other causes of ulceromembranous lesions, such as diphtheria and syphilis. Probably in a majority of cases the experienced observer may make the correct diagnosis by clinical signs alone; but this should always be substantiated by all the tests outlined in the case here reported.

The prognosis is good in a great majority of the cases. The ulcers remain superficial and heal in a few days without scarring. They sometimes last for weeks, however, and if the ulceration has been deep, scarring will probably result. In the debilitated or when occurring in the course of a leukemia, the necrosis is prone to become very extensive and may prove fatal, death resulting from exhaustion or secondary septic complications.

The treatment is usually simple. Locally chromic acid (5 per cent.), zinc sulphate (5 per cent.), silver nitrate (10 per cent.), tincture of iodin, or trichloracetic acid may be used. I have found chromic acid the most efficacious of all these. The last two should be used only on small ulcerated surfaces. General treatment is almost always indicated, and will be suggested by the individual case. Good food, regular habits, and, above all, the care of the mouth are essential. If the gums and teeth

are allowed to remain in bad condition, local applications to the lesions may be without effect, as a constant supply of Vincent's organisms may be furnished from these sources. A good dentist is one of the best of therapeutic measures. In cases in which these simple measures do not suffice or in which the necrosis extends rapidly or deeply, salvarsan or one of the other arsenomercurial compounds should be given. They appear to be as specific for this form of spirochetal infection as in syphilis, for the lesions heal with wonderful rapidity after their use.

CONTRIBUTION OF DR. ARIAL W. GEORGE, DR. RALPH D. LEONARD, AND DR. FREDERICK W. O'BRIEN

THE ROENTGEN DIAGNOSIS OF DISEASE OF THE UPPER RIGHT ABDOMINAL QUADRANT

The Anatomy of the Duodenum and Its Relations; Duodenal Ulcer; Comparison of the Direct Method with the Roentgenoscopic or Indirect Method; the Second Portion of the Duodenum; The Gall-bladder; Technic; The Large and Small Bowel; Value of Roentgen Evidence in Gall-bladder Disease.

From a roentgenologic point of view the upper right abdominal quadrant has become one of the most important somatic areas which we are called upon to study. We have included in this review of our findings the first and second portions of the duodenum, the biliary tract, and certain secondary influences upon them as reflected in changes noted by us in the small and large bowel.

It is with pardonable pride that we state that the positive advances made during the past ten years in the roentgenologic diagnosis of disease of the duodenum and gall-bladder are distinctly an American contribution to medical science made possible by the extensive use of the plate method in contradistinction to the roentgenoscopic (fluoroscopic) method employed by Continental workers.

We gratefully acknowledge the early work of Holzknecht, Haudeck, Schwartz, and others for supplying the stimulus for our later work, but to Cole, of New York, must go the major part of the credit for the progress made by American Roentgen workers in the field of gastro-intestinal diagnosis. His early work on duodenal lesions has not been surpassed up to the present time. It has been our good fortune to have followed Cole's

methods not blindly but judiciously we think, and to him we are indebted as well as are other workers for having learned to properly interpret the densities of the upper right abdominal quadrant as registered by the *x*-rays, not alone in duodenal lesions, but in our more recent efforts to interpret gall-stone shadows and the visualized gall-bladder itself.

The Anatomy of the Duodenum and its Relations.—An appreciation of the normal anatomy of the duodenum and its relations

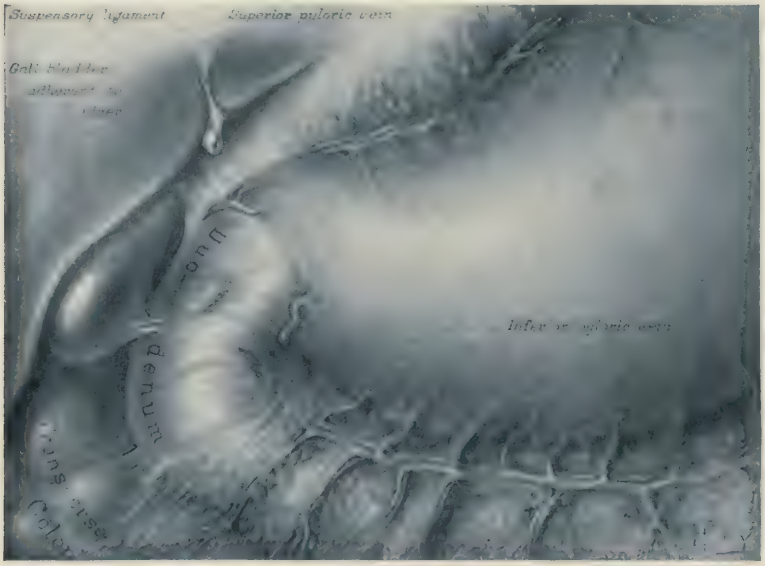


Fig. 106.—Showing external surface of ulcer of anterior wall of the duodenum (W. J. Mayo).

is necessary for proper perspective. "The duodenum was originally named so because its length was supposed to correspond to the breadth of twelve fingers placed side by side. Its shape is approximately that of a horseshoe, the concavity toward the left accommodating the head of the pancreas. It commences at the pylorus and extends to the duodenojejunal flexure.

It may be divided into a superior portion, a descending portion, and an inferior portion. The superior portion is the first part of the duodenum and runs almost directly from before backward to become continuous with the nearly vertical de-

scending portion at the superior duodenal flexure. The inferior duodenal flexure connects the descending with the inferior portion, the upper portion of the latter being almost horizontal and forming what is sometimes termed the horizontal portion of the gut, while its termination bends upward and to the left, forming the ascending portion.

Fig. 107.—Normal stomach.

The relations of the duodenum are somewhat complicated. It is in contact with the following organs: the stomach and gall-bladder (superior portion), the liver (superior and descending portion), the pancreas (concavity of the descending portion), the inferior vena cava, the right kidney and suprarenal body (descending portion). The inferior portion lies in front of the vertebral column and aorta and behind the root of the mesentery. The superior and shortest portion is the only part of the

duodenum which is situated directly behind the abdominal anterior wall as the direct continuation of the stomach, the descending portion being concealed by the transverse colon and the inferior portion being in contact with the posterior abdominal wall behind the mesentery. The superior mesenteric vessels pass in front of the inferior portion, and the portal vein, arising behind the head of the pancreas, is posterior to the superior portion.

In general, the duodenum presents the typical characteristics of the small intestine, and especially those of the jejunum, its

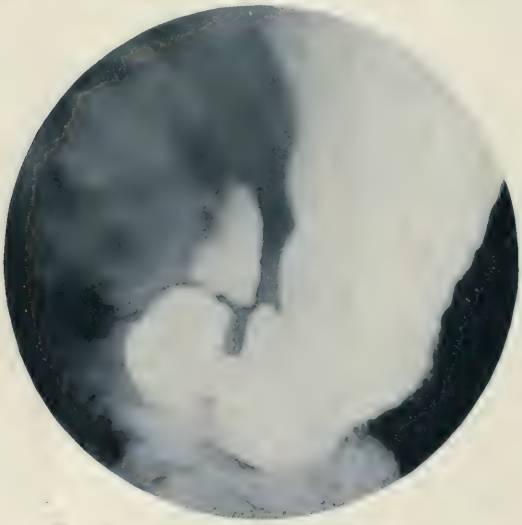


Fig. 108.—Normal stomach, lateral view.

peculiarities, in addition to its situation and relation to the peritoneum, being as follows: its superior portion has no valvulæ conniventes, as these do not make their appearance until the superior duodenal flexure is reached; in the submucosa of this superior portion, however, large numbers of duodenal (Brunner's) glands occur. . . . The descending portion contains the orifices of the common bile-duct and of the pancreatic duct. . . . Both ducts usually unite shortly before their termination, causing a slight elevation characterized by delicate folds of mucous mem-

brane, the duodenal diverticulum (diverticulum of Vater). With the exception of its position and relations to the peritoneum the inferior portion of the duodenum differs in no respect from the jejunum, into which it passes without demarcation at the duodenojejunal flexure. The layers of the duodenal wall are similar to those of the small intestine in general (Sobotta and McMurrich).

Duodenal Ulcer.—Since 95 per cent. of all duodenal ulcers are found in the first or superior portion of the duodenum, the diagnosis of duodenal ulcer by the Roentgen ray is now the simplest procedure of any connected with the diagnosis of the pathology of the upper right abdominal quadrant provided one will follow what we have been pleased to call the direct method.

It offers no particular difficulty other than care in technic because it is based upon the following proved data: Anatomically the first portion of the duodenum is a constant entity which can always be demonstrated on an *x*-ray plate with characteristic shape and outline without exception if it is normal. Any constant defect in contour means a pathologic condition.

The direct method is opposed to the conception of the symptom complex of the European school which emphasizes inferential evidence. In the direct method no little effort must be made to show the anatomic condition of the first portion of the duodenum. No set rule can be laid down as to how this can be accomplished. Plates should be made with the patient in the prone position first, and in the majority of cases the first portion of the duodenum should be visualized readily, its borders appearing smooth and without contractures, in general appearance not unlike a bishop's miter.

In the average case it is simple, but occasionally spasm of the pylorus, pressure from adjacent viscera, and pathologic conditions, as gall-stones, diseased gall-bladder, and reflexes from a chronically diseased appendix will be the cause of an imperfectly filled or deformed duodenal bulb.

Whenever such is the case the examination must be carried over a sufficient period of time to satisfy one's self that the bulb has had time in which to fill. Most important of all, the patient

should be examined on the right side and a view of the duodenum obtained in this position. If one does not meet with success by this maneuver, then visualization of the first portion must be tried with the patient upright.

If the first portion of the duodenum cannot be outlined in its entirety in any of these positions, one may safely assume pathology; for if it be admitted that with a series of plates a normal duodenal bulb can be shown when it is normal, then the converse of the proposition must be true.

Fig. 109.—Chronic ulcer of the duodenum.

Many duodenal ulcers at operation have been demonstrated as mere mucosal defects, so that some workers were disinclined to believe the deformity of the duodenal bulb as pointed out by Cole and ourselves could be indicative of such mucosal erosions. It is now recognized, however, that in this type of ulcer the amount of callus in the submucosal, muscular, and peritoneal coats belies the mucosal defect itself, which accounts for the roentgenographic appearance of these ulcers, which seems exaggerated in comparison with the operative findings. In no other part of the gastro-intestinal tract is the deforming effect

produced by scar-tissue upon the opaque mass so marked as in the first portion of the duodenum.

In many cases on the Roentgen plate opposite the ulcer will be seen an incisura partly spastic in character, partly due to the involvement of the deep muscle layers by cicatrix. The pitfall for the novice in the Roentgen study of the duodenum is the differentiation of the deformity due to ulcer from that due to adhesions. Differentiation can be made readily between simple

Fig. 110.—Chronic ulcer of the duodenum.

adhesions and ulcer. But where one finds a combination of ulcer and adhesions one cannot say always, nor is it necessary, whether these adhesions are due to the ulcer or to gall-bladder disease, or to both. It is sufficient to pass the opinion that there is a surgical lesion.

In simple adhesions the deformity of the opaque mass will be found to be greater at the beginning of the examination, decreasing as the stomach empties, and while the stomach when first filled will be found drawn over to the subhepatic region,

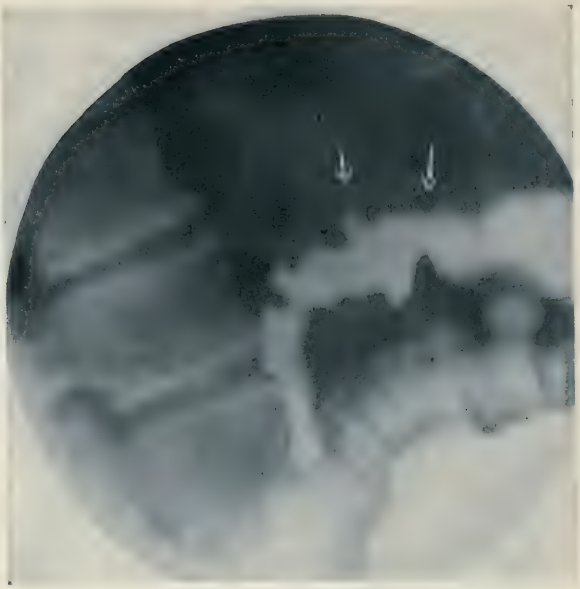


Fig 111.

Fig. 112.

Fig. 113.

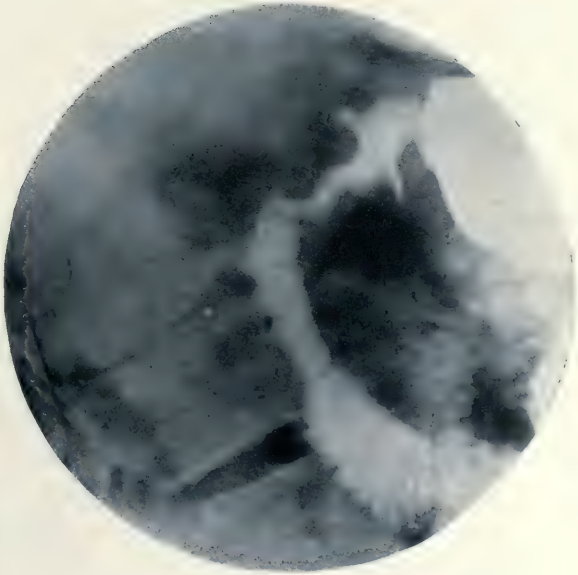


Fig. 114.

Figs. 111–114.—Chronic ulcer of the duodenum, lateral view. Figures 113 and 114, made six months after Figs. 111 and 112, show increase in the amount of scar tissue about the first portion of the duodenum.

successive plates will demonstrate it moving back to the median line as it empties. When the degree of deformity remains the same from the beginning of the examination until the stomach has almost emptied itself it is more characteristic of ulcer. A constant deformity of the duodenum is peculiar to ulcer and to no other lesion.

That a normal first portion of the duodenum rules out surgical ulcer increases many times the negative value of a Roentgen diagnosis by serial plates. Whenever we demonstrate the first portion of the duodenum to be free from deformity we pass a negative opinion. Once only in our experience was our opinion unconfirmed at operation up to date. Much of the usefulness of roentgenologic examination depends upon this negative aspect.

We find, then, that the Roentgen diagnosis of duodenal ulcer by the direct method basically rests upon the demonstration by serial plates of the continuity of the first portion of the duodenum or the demonstration of a constant defect in its contour. There is no better argument for the plate method than that this can be accomplished unfailingly with a careful and exact technic.

The roentgenoscopic or indirect method when applied to the study of the duodenum is entirely unsatisfactory. It is true that occasionally the duodenum can be seen in its entirety, but it can never be seen for a long enough time to satisfy one as to its anatomic completeness. It certainly cannot be shown in all cases, especially in well-nourished individuals. Furthermore, in the standing position in which the roentgenoscope is ordinarily used this demonstration is usually impossible. We do not mean to infer that the roentgenoscopic study of the gastro-intestinal tract is worthless. The roentgenoscope has undoubtedly its use in the study of the stomach and the large bowel. In the study of the duodenum and, much more so, the gall-bladder the roentgenoscope must really be considered as of minor value. The plate method is a more tedious process than the roentgenoscopic method, but the accurate results obtained by the former outweigh any other consideration.

The *second portion of the duodenum*, as seen with the use of

the barium buttermilk meal, is about the width of the adult thumb and does not show on the Roentgen plate the smooth contour of the bulbus duodeni, but rather a characteristic serrated appearance due to the valvulæ conniventes. Occasionally it is dilated to a greater width than this, which may be merely anatomic. When dilated to any considerable degree it is always due to obstruction somewhere beyond the second portion. Rarely have we found the constriction of the second portion of the duodenum to be due to gall-bladder adhesions, though the lumen may be considerably narrowed by adhesions. In the case of adhesions, however, the function of the second portion of the duodenum is not altered so far as the passage of the opaque meal is concerned.

We have found the second portion of the duodenum of chief interest as a very important diagnostic sign in the study of gall-bladder disease. It may be the only evidence by which we can exactly localize the size and shape of the gall-bladder. We have frequently found the second portion of the duodenum picked up, as it were, by adhesions to the gall-bladder, so that the gall-bladder outline could be distinctly made out by this relation. When the descending or second portion of the duodenum instead of passing directly downward is seen to pass outward toward the liver border, then curve to its normal position, this may be considered almost pathognomonic of gall-bladder disease.

A sign of secondary importance described by a few observers is the filling of the ampulla of Vater by the opaque medium. It does not occur commonly, and may indicate disease of the gall-bladder, the assumption being that if the opaque meal enters the ampulla and is retained there for any reasonable length of time, so may food, and if such food is retained, there is a very definite potential danger of ascending infection of the gall-bladder.

The Gall-bladder.—The text-books on anatomy locate the gall-bladder in a fairly definite and constant position. We have found, however, from a study of our plates, which without question show the gall-bladder shadow, that the gall-bladder may be

found most anywhere on the right side below the diaphragm. We have seen it apparently lying over the spine in the median line, toward the outer side in the right flank, and even below the crest of the ilium almost in the true pelvis.

It must be borne in mind that a large percentage of gall-bladders have a distinct mesentery of their own which allows considerable latitude in movement. The anatomists are inclined to give the contrary impression that the gall-bladder is adherent to the under surface of the liver and firmly fixed.

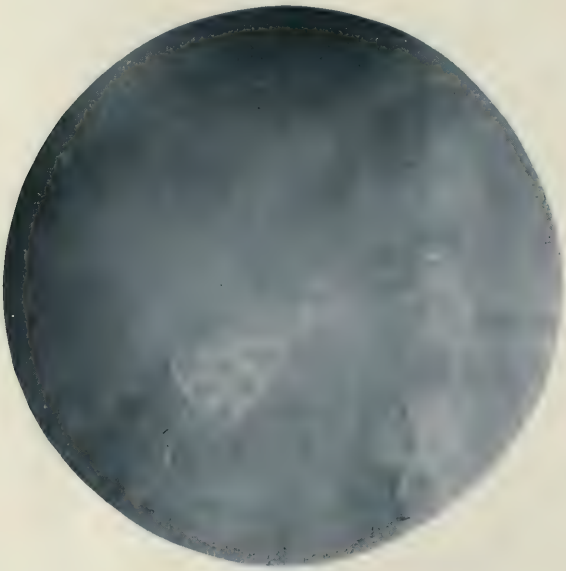


Fig. 115.—Group of gall-stones.

The size of the gall-bladder shadow as we see it is also a variable factor. In the dissecting room the apparently normal gall-bladder is about 1 inch in diameter and 2 to 3 inches in length. The Roentgen shadow of demonstrated gall-bladders varies from the size of an olive to the size of a grape-fruit, as in hydrops.

The visualized gall-bladder is roughly pear shaped, the most constant feature being the characteristic curve of the lower pole.

The inner edge of the shadow is usually distinct. This fact is a help in differentiating between a gall-bladder and a kidney shadow.

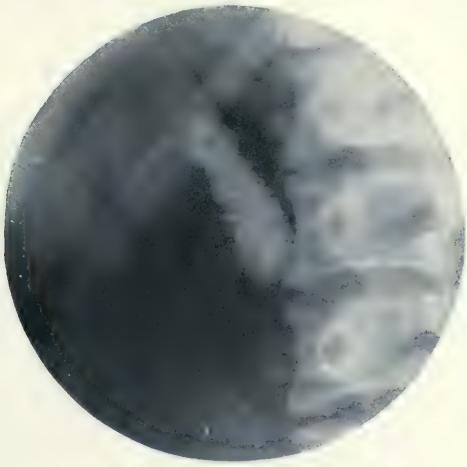


Fig. 116.—Group of gall-stones.

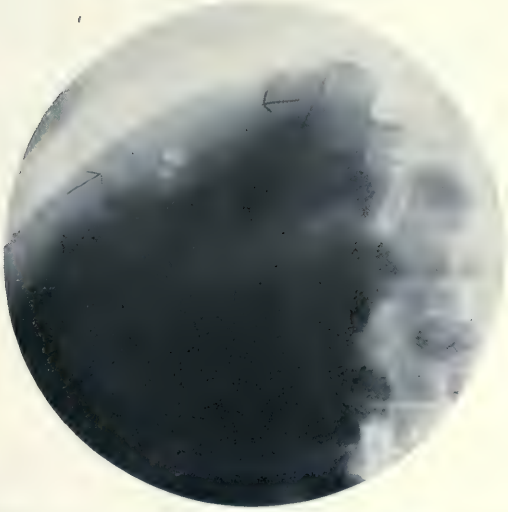


Fig. 117.—Pathologic gall-bladder and two small stones.

As a result of our observations we have assumed as a working hypothesis that only when some pathologic change has taken place either in the walls of the gall-bladder or its contents can

its shadow be demonstrated on the *x*-ray plate. We also assume the converse that for practical purposes the shadow of a normal gall-bladder cannot be demonstrated.

The diagnosis of gall-stones by the Roentgen ray we simply mention here for completeness, and to show its relation to our later work in the diagnosis of gall-bladder disease without stones.

Fig. 118.—A group of stones with more or less fixation of the small bowel about the gall-bladder, and with marked ptosis of the stomach.

Our conclusions reached in 1915 and reported at length at that time we have not yet found it necessary to change, in effect that with proper technic gall-stones can be demonstrated by the *x*-ray whenever present. Stones containing calcium may be demonstrated with ease, while the so-called soft stones can be demonstrated with care.

While perfecting the technic and our methods of gall-stone diagnosis, we were led to use the term "suspicious shadows"

in reporting our results in cases where we recognized changes in densities in the plate not definite enough to warrant a positive diagnosis of gall-stones and yet preventing an absolutely negative opinion.

This term "suspicious shadows" aroused a great deal of adverse criticism from our colleagues, on the ground that it was elusive and perhaps a dangerous phrase to use.

Fig. 119.—Outline of gall-bladder filled with calcified crystals. Note the "picking up" of the hepatic flexure by adhesions.

As a result of our endeavor to interpret properly the significance of these so-called "suspicious shadows" has come forth our conviction that the gall-bladder can when pathologic, and then only, be demonstrated by the *x*-rays.

We early observed that in the majority of instances these shadows or changes in density were not due to gall-stones, but rather were shadows from organs occupying the right upper quadrant, as the quadrate or caudate lobes of the liver, gall-

bladder, upper pole of the kidney, adrenal gland, and food-filled duodenum or stomach antrum. By repeated examinations of the upper right abdominal quadrant with the subject fasting, with the stomach and duodenum barium filled, and by persistent study of kidney plates we were able to differentiate these sus-

Fig. 120.—Pressure of the gall-bladder on first portion of the duodenum.

picious shadows. Bearing in mind the appearance of the gall-bladder in cases with self-evident stones also aided in demonstrating the characteristic density which we now interpret as the pathologic gall-bladder.

By "pathologic" we mean either the walls of the gall-bladder are thickened or the bile content is of greater density than nor-

mal, or greater in quantity, or it contains stones or foreign material of some sort. Furthermore, there may be changes in the circulation, congestion in blood-vessels, or unknown alterations which singly or in combination are sufficient to make a visible contrast between the gall-bladder shadow and the shadow of surrounding tissues.

Let it be borne in mind that we offer this simply as a working hypothesis. Thus far, judging from our operated cases, we consider it a safe and reliable diagnostic aid. We shall gladly

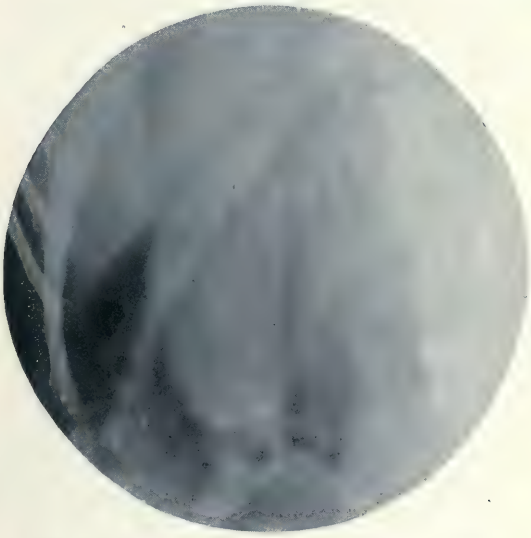


Fig. 121.—Pathologic gall-bladder without stones.

admit the unreliability of this hypothesis once it is demonstrated that the normal gall-bladder can be visualized.

To declare that a normal gall-bladder can be visualized and offer in proof of it that cases have come to operation wherein the surgeon has passed the opinion that the gall-bladder was normal, can hardly obtain our serious thought.

We are sure it has been the experience of every busy surgeon that on more than one occasion he has failed to detect sizable gall-stones within the gall-bladder on mere palpation. Nor do we believe that any surgeon of note today would declare that

no pathology was present in a gall-bladder because on inspection no gross disease was recognized.

So when claims are made that the normal gall-bladder can be shown on the plate we shall deem such worthy of attention when accompanied by a negative report from the pathologist, for only by removal of the gall-bladder and subjecting it to a

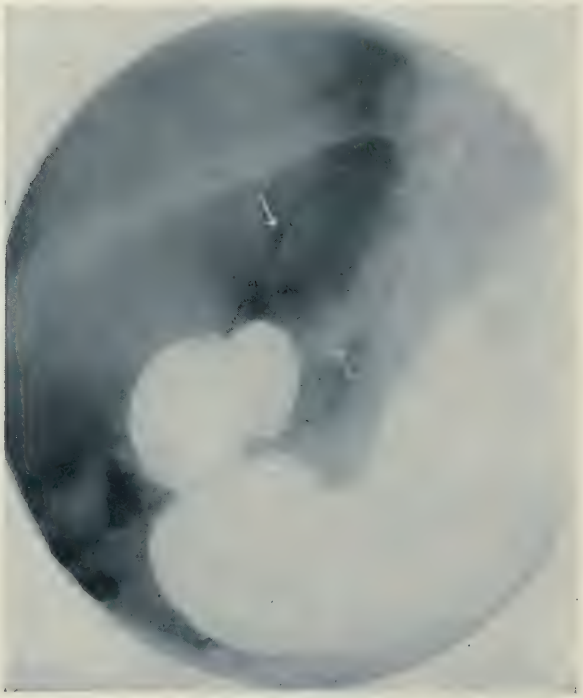


Fig. 122.—Pathologic gall-bladder without stones.

microscopic examination can the absence of disease be ascertained.

Some Roentgen workers claim to have visualized the gall-bladder in normal healthy individuals, to which we answer that as a certain number of "normal" individuals may show gall-stones, so too any series of "healthy" persons will unquestionably have technically pathologic gall-bladders without clinical symptoms. In these cases the bile may be slightly abnormal

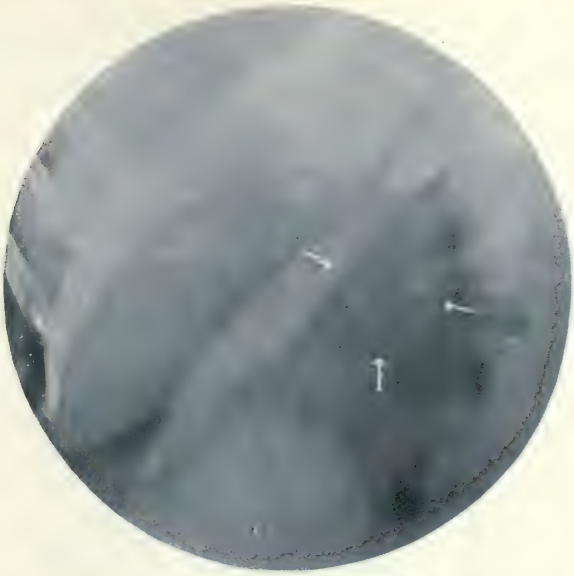


Fig. 123.—Pathologic gall-bladder.

Fig. 124.—Pathologic gall-bladder without stones.

in consistency or there may be changes in the gall-bladder walls due to some old typhoid, streptococcus, or colon infection of the gall-bladder long since forgotten.

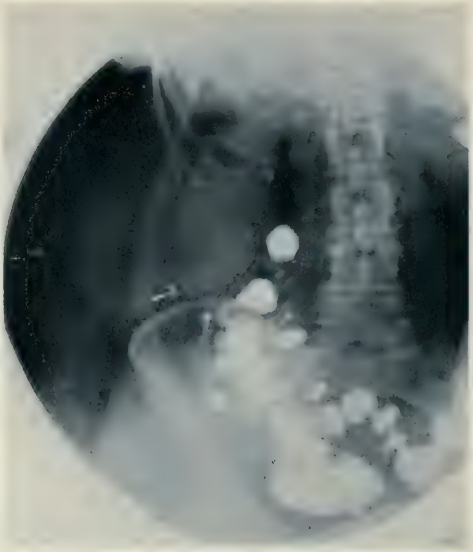


Fig. 125.—Hydrops gall-bladder.

Fig. 126.—Pathologic gall-bladder with marked adhesions about the second portion of the duodenum.

It is clear, therefore, that any experimental work done on a series of "ordinarily healthy" individuals to prove the possi-

bility of the Roentgen demonstration of the normal gall-bladder is to no purpose. Furthermore, a certain amount of work has been done upon the cadaver tending to prove the fallacy of our hypothesis, but roentgenologists of any experience know that results obtained in the Roentgen examination of the dead cannot be translated to the living, so that we consider such work worthless as far as offering any aid in the solution of the problem is concerned.

Fig. 127.—Pathologic gall-bladder with "picking up" of hepatic flexure by adhesions.

We do not question the possibility that the time may arrive when the normal gall-bladder will be demonstrated on the *x*-ray plate. Meanwhile we believe we have found a satisfactory working hypothesis substantiated by our experience and rational in its theory.

Technic.—The first requisite for a proper Roentgen examination in suspected gall-bladder disease is that the patient be examined when fasting. And it is further important that the patient should not have eaten a solid meal or, in fact, have

taken too much liquid within six hours, for food or liquid in either the first or second portion of the duodenum is apt to give

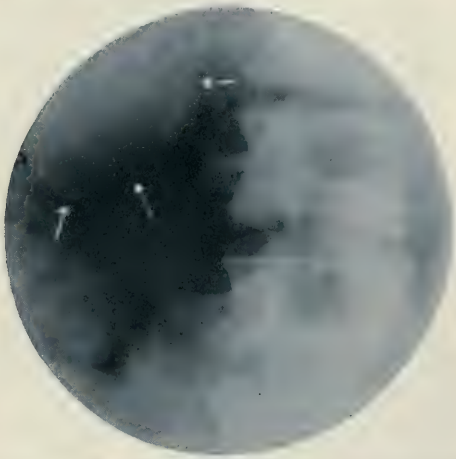


Fig. 128.—Pathologic gall-bladder containing one large stone.

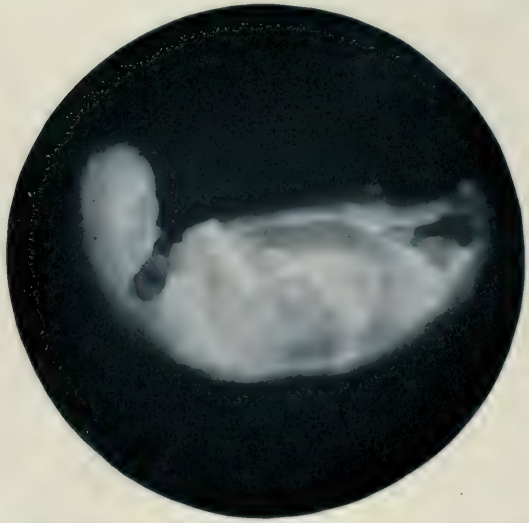


Fig. 129.—Same case as Fig. 128 Plate made after removal of gall-bladder.

rise to confusing densities on the plate. The patient should be examined prone, lying face downward on the table, with the

plate or intensifying screen and plate beneath so arranged that the costal margin will bisect the middle portion of it.

A small cylinder and diaphragm preferably of the size supplied by the Kelley-Ket Company for frontal sinus work should be employed, and so arranged above that the costal margin bisects the area of the cone. The distance of the tube from the plate is not of the utmost importance. We find that using the

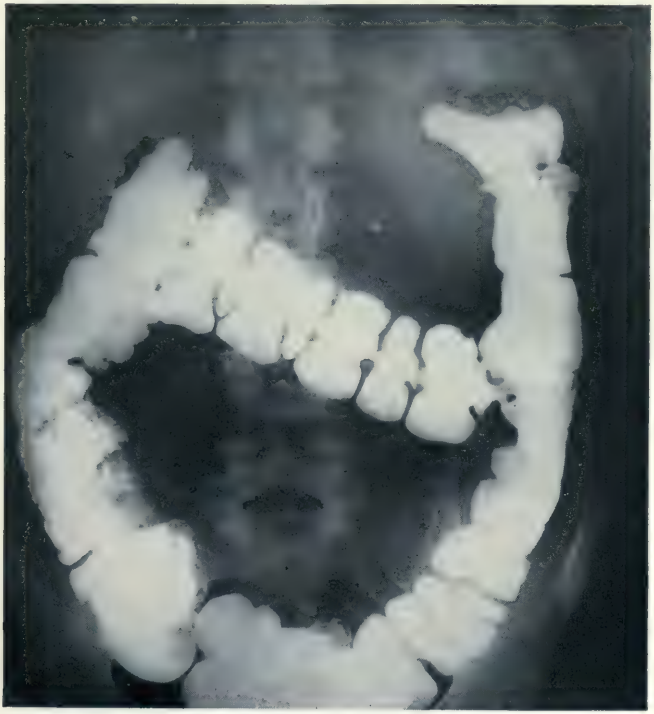


Fig. 130.—Pathologic gall-bladder "picking up" the hepatic flexure.

cone 3 or 4 inches above the back of the patient appears to help in giving a larger and clearer image. The exposure and its intensity must vary with the individual patient. Not the least important thing is to make a sufficient number of plates with the patient in the one position. It is a mistake to try to distort the shadows in the upper right abdominal quadrant. Plates should be developed as they are taken, and studied while in

development as well as when finished. We have found that in a great many cases the outline of the gall-bladder was seen during the development better than when the plate was completely fixed and dry.

We cannot insist too strongly on the matter of making a sufficient number of plates in the one position and with the

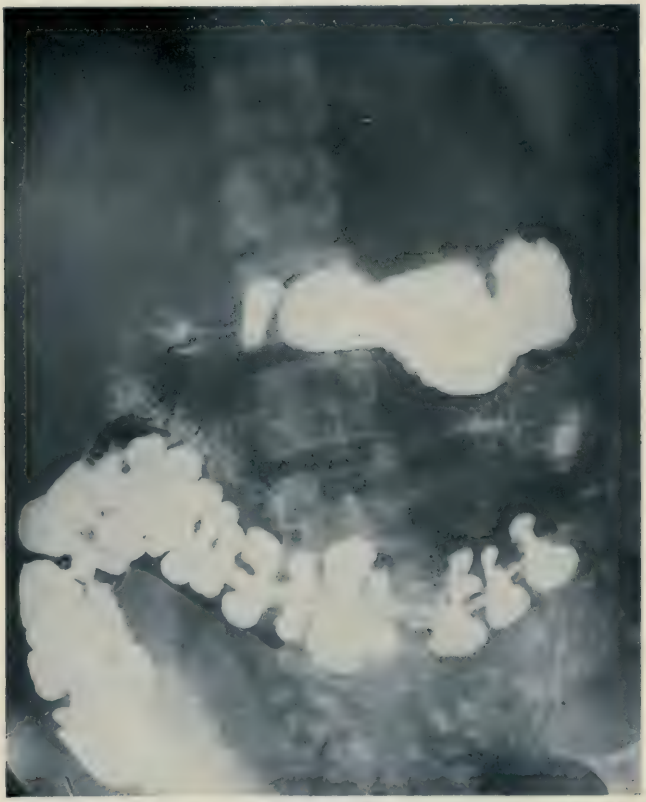


Fig. 131.—Fixation of second portion of the duodenum to gall-bladder.

gastro-intestinal tract empty. In fact, we feel that the reason other workers have not had the success which we believe possible is due to this very fact. This will explain especially, we believe, the failure in hospital clinics as opposed to private work. The technic just described is quite as necessary and important for

the diagnosis of gall-stones as for any other suspected pathologic condition of the gall-bladder.

We have made this technic just described a routine measure in all gastro-intestinal cases sent to us for diagnosis. Once we have determined as much about the right upper quadrant as we feel we can in this manner, the patient is then given the barium-buttermilk meal for visualization of the gastro-intestinal tract. Following the direct and indirect examinations of the stomach

Fig. 132.—Hydrops of gall-bladder with one stone in cystic duct.

we then pay particular attention to the barium-filled duodenum in relation to the densities seen in the upper right quadrant, and still again in the six-hour and twenty-four-hour examination of the bowel, for we have found that we often obtain valuable signs pointing to gall-bladder disease at these times. It should be here recalled what we have said above, that the gall-bladder may be found almost anywhere to the right of the median line below the diaphragm, and hence in occasional cases search will have to be made for it in other than its usually given location.

The Large and Small Bowel.—In conclusion, we desire to call attention to a recent observation we have made in gall-bladder disease suggested by the transposition of the jejunum to the upper right quadrant. In gall-bladder disease considerably more gas will be found in plates made of the upper right quadrant than is seen normally, and a careful study of the plates will reveal the fact that this may be in the small bowel (jejunum)

Fig. 133.—Gall-bladder after removal.

rather than in the hepatic flexure or transverse colon. This observation must be checked up by comparison of the plates made before and after taking the barium meal. The appearance of the gas-filled hepatic flexure and transverse colon as seen in the six- and twenty-four-hour plates made following the barium meal is quite characteristic in gall-bladder disease. It appears on the plate like a sacculation of gas with a faintly limned periphery of barium just above which or impinging upon it can be seen the visualized gall-bladder.

While the diagnosis of duodenal ulcer has now passed without the realm of controversy, not so the value of Roentgen evidence in gall-bladder disease, but just as the early work of Cole and ourselves on duodenal ulcer was severely questioned, only ultimately to be accepted, so we feel that our present position on the evidence of gall-bladder pathology is based on scientific grounds, and will be accepted as such.

CLINIC OF DR. JOHN B. HAWES, 2D

MASSACHUSETTS GENERAL HOSPITAL

EARLY DIAGNOSIS OF PULMONARY TUBERCULOSIS

The Need of Diagnostic Standards in the Early Diagnosis of Tuberculosis. Importance of the History and Constitutional Signs and Symptoms as Compared with Those Referred to the Lungs. Definitions of Certain Terms. The Need of Thoroughness and Especially Common Sense.

December 17, 1917.

DESPITE the activity and efficiency of the campaign against it, our tuberculosis problem is still with us. The present war has brought to light many hitherto unsuspected cases, while, in addition, the stigma of tuberculosis has been cast on not a few who later turn out to be suffering from something else. Tuberculosis in some form or other and problems connected with it constitute a large part of the work of every physician who does general practice, and no such physician can do justice to his patient or to himself unless he is able to diagnose tuberculosis in its early stages. There is urgent need, therefore, especially at the present time for us to formulate and, if possible, standardize our ideas as to the early diagnosis of this disease.

To many physicians any such standardization may seem quite unnecessary. Just as the diagnosis of malaria is based on the finding of the plasmodium in the blood, and that of typhoid fever on a positive Widal reaction or blood-culture, so the early diagnosis of tuberculosis is based on certain combinations of signs and symptoms. These, without the slightest hesitation, any physician or, indeed, medical student would enumerate somewhat as follows:

1. Family and personal history.
2. History of exposure.

3. Constitutional signs and symptoms, such as—
   (*a*) Loss of weight.
   (*b*) Loss of strength.
   (*c*) Fever.
   (*d*) Rapid pulse, etc.
4. Local signs and symptoms referred to the lungs or the chest, such as—
   (*a*) Hemorrhage.
   (*b*) Pain or pleurisy.
   (*c*) Cough and sputum.
   (*d*) Dulness, altered voice and breath sounds, râles, etc.

It is very easy to formulate such a list as this of the signs and symptoms on which a positive diagnosis may be based. On more careful analysis, however, one is immediately confronted by the fact that there is a tremendous difference of opinion as to what these terms, such as "fever," "hemorrhage," etc., really mean, and on what combination of signs and symptoms a positive diagnosis in the absence of tubercle bacilli in the sputum should be based. One group of men will demand certain signs in the chest without which no diagnosis should be made; other physicians believe that a careful study of constitutional signs and symptoms will bring about more accurate results, even if there are few or no abnormal signs in the lungs; a third group of physicians depends on *x*-ray evidence, while a fourth group puts reliance on tuberculin tests, etc.

Again, referring to the signs and symptoms themselves, ask any twelve physicians what each one means by the word "hemorrhage," and you will be apt to get a dozen different answers. Ask what constitutes "fever" or "rapid pulse," and no two will agree, or again, ask what "loss of weight and strength" means, and you will find the same variance in the answers. It is evident, therefore, that despite the need for this, there is at present no definite set of standards on which the early diagnosis of tuberculosis can be based, and it is likewise evident that any attempt at such standardization will be difficult.

Attention was recently focussed on this subject in carrying on the tuberculosis experiment in Framingham, Massachusetts.

This "experiment," now well known as a "Community Health and Tuberculosis Demonstration," has been financed by the Metropolitan Life Insurance Company of New York for a three-year period, and is being conducted under the supervision of the National Association for the Study and Prevention of Tuberculosis. One of the first difficulties that Dr. Donald Armstrong, the executive officer, and Dr. P. C. Bartlett, his medical director, met was in regard to this question of early diagnosis. There was no consensus of opinion among the physicians of Framingham as to what constituted sufficient evidence for a positive diagnosis. Consequently, a committee of Boston physicians was asked to prepare a set of standards for this purpose. In formulating a draft of such standards, which I was asked to prepare for this committee, I at once found it necessary to define certain terms mentioned above, such as "hemorrhage," "fever," "loss of weight," etc.

The following cases illustrate the various combinations of signs and symptoms on which a definite diagnosis may justly be based. In connection with them I will discuss the definitions and diagnostic standards adopted for the purposes of the Framingham Experiment.

DIAGNOSIS BASED ON HEMORRHAGE

CASE 1.—This man, thirty-five years old, previously healthy, had been feeling perfectly well, when he suddenly had a fairly profuse hemorrhage of 2 or 3 tablespoonfuls of blood. His family and personal history are negative, and there is little to be found in the lungs. I have told him that beyond the slightest doubt the hemorrhage was due to tuberculosis and that he must keep very closely under my supervision. I hope to persuade him to go to a sanatorium for a while at least.

In this case there has been a frank and definite pulmonary hemorrhage, and the diagnosis of tuberculosis is absolutely justified even if the signs in the lungs are very slight and the sputum negative.

CASE 2.—This patient comes to the clinic because she has had frequent small hemorrhages. She has seen many doctors in

New York and Philadelphia and has been told that she has consumption. Her general condition is excellent, and I can hear nothing abnormal in the lungs. Her teeth are in very poor condition, the gums spongy, with marked evidence of Rigg's disease. On careful inquiry I found that the so-called "hemorrhages" consist of minute spots or streaks of blood, never as much as a teaspoonful. I have advised her to go to a good dentist to have her teeth attended to and her gums treated. This she did some time ago, since which time the hemorrhages have ceased.

Here the patient had what she called a "hemorrhage" and repeated ones. Impression had been given her that she had consumption, on account of which she has been put to much unnecessary expense and anxiety.

CASE 3.—A few weeks ago this patient, a strong, robust Irish girl, weighing over 160 pounds and the picture of health, came to see me because for a great many years at frequent periods throughout the year she has raised blood in considerable amounts up to 1 or 2 tablespoonfuls. The last hemorrhage was three weeks ago. In taking her history, her mother told me that when a young girl she had swallowed a stick-pin and that she had never been able to recover it. On examination I found very little in the lungs, no râles, and few other abnormalities, but on account of this history of having swallowed a stick-pin, which I thought might have gone into the lung instead of into the stomach, I have had an *x*-ray examination made. The plate clearly shows a foreign body at the base of the right lung, but also suspicious shadows at the left apex. This girl is in perfectly good condition and has simply been worried on account of the hemorrhages.

This is a difficult proposition. Constitutional signs and symptoms are absolutely lacking, and yet there is this history of repeated hemorrhages. Perhaps there is an inactive tuberculous process at the left apex in addition to the inflammatory changes set up around the foreign body, although I can hear no râles or other signs of activity. It seems to me that the burden of proof, however, is distinctly on anyone who maintains that this patient is at present suffering from active pulmonary tuberculosis.

These 3 cases show how indefinite a term is the word "hemorrhage." The definition adopted by our committee is as follows:

> "Any amount of expectorated blood, with or without sputum, requires medical investigation as to its source. Blood-streaks, blood-spots, etc., may or may not mean tuberculosis. On the other hand, a hemorrhage of 1 or 2 teaspoonfuls is presumptive evidence of the disease."

This definition seems to me sane and sound and one that might well be universally adopted.

DIAGNOSIS BASED ON CONSTITUTIONAL SIGNS AND SYMPTOMS

CASE 4.—This woman is a nurse, thirty years old, and she comes to the clinic on account of loss of weight and strength and because she is not able to do her work as well as she could a year ago. She has a slight cough, but no sputum. Temperature and pulse are normal. She weighs 120 pounds, which is 18 pounds less than what she weighed six months ago. In the lungs I find nothing but a "suspicious right apex." There are a few other suspicious signs and symptoms. I have told her that I believe that she has incipient tuberculosis and that she must report regularly to me every two weeks and be prepared to go to a sanatorium unless she improves.

The striking point in this case is loss of weight and strength, but here, again, we are using terms that need some sharp definition. What may constitute "loss of weight" in its pathologic sense to one person may mean something entirely different to another.

Our definitions of these two terms are as follows:

> "Loss of Weight: By 'loss of weight' should be understood an unexplained loss of at least 5 per cent. below normal limits for that particular individual within four months' time."
>
> "Loss of Strength: By 'loss of strength,' in its pathologic sense, is meant undue fatigue and a lack of staying power which are unusual for the individual patient and which cannot be satisfactorily explained."

These definitions may require some modification to meet individual cases. On the whole, however, they seem to be working out fairly satisfactorily in Massachusetts.

DIAGNOSIS BASED ON FEVER AND RAPID PULSE

CASE 5.—This man, who is twenty-seven years old, is sent to me for examination by his employer. His family and personal history are not very remarkable, but suggest tuberculosis. The examination of the lungs shows comparatively little. The temperature and pulse, however, taken quietly four times a day at home over a period of three or four days show a slight afternoon fever and a pulse averaging 90. This fever and rapid pulse in combination with other signs and symptoms justify me in making a definite diagnosis. His chart is as follows:

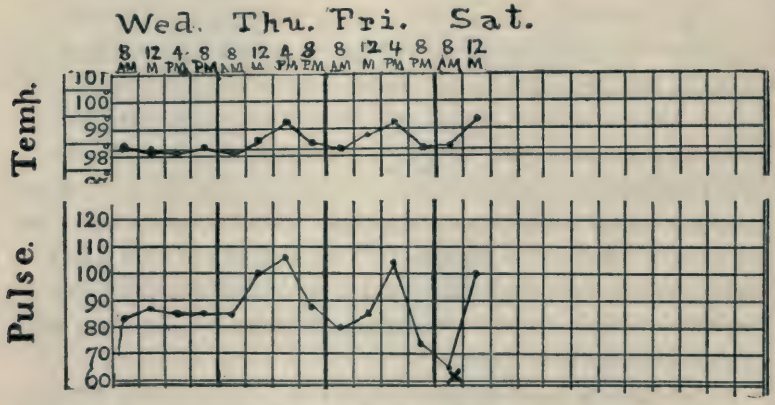


Fig. 134.—Taken lying down.

I cannot emphasize the importance of such a combination as this—slight fever and rapid pulse. It *may* not mean tuberculosis, but in many cases it certainly does.

CASE 6.—This young man, a draftsman of twenty-two, comes to the clinic because he has had a cough off and on for a year, and especially because he has lost weight and strength, and in other ways does not feel as well as he thinks he should. He is evidently an intensely nervous person. At my first examination he had a temperature of 100° F. and a pulse of 122. Aside from this I could find very little abnormal. I told him to take his temperature and pulse four times a day at home, which he did. The pulse ranged from 60 to 70, and the temperature was constantly normal. Backed up by this evidence I am prepared to tell him

definitely that I do not believe that he has active pulmonary tuberculosis.

In this instance the patient complains of loss of weight and strength and other constitutional symptoms. The fever and rapid pulse at his first examination at the clinic are not more than that of many patients of a nervous temperament under similar circumstances. I consider the normal temperature and slow pulse taken at home to be evidence that more than counterbalances the history of cough and slight loss of weight and other symptoms of which this patient complains.

Our definition of fever and elevation of pulse as illustrated by these cases is as follows:

> "Fever: An occasional temperature of 99° F. should not be considered 'fever.' A temperature which persistently runs over 99° F. when taken at least four times a day over a period of one week (by mouth, five minutes) should be considered of significance and to constitute 'fever'."
>
> "Elevation of Pulse: Where the average normal pulse of the patient is already known, an elevation of 15 beats per minute when the pulse is taken quietly at home during various periods of the day should be considered abnormal. In cases where the average pulse is not known, and, of course, this constitutes the majority of cases, one should consider an average pulse of 85 or over in men and 90 or over in women to be abnormal. The combination of a subnormal temperature and an elevated pulse as defined here should be considered of great importance."

I have found these definitions helpful to me in my work in closely limiting what were before loose and indefinite terms.

DIAGNOSIS BASED ON FAMILY HISTORY AND EXPOSURE

It is unnecessary to cite cases illustrating these points. There is urgent need, however, of sanity in weighing such evidence. Because an uncle, aunt, grandparent, or cousin has died of consumption does not mean that the patient in question must have it or has even been exposed to it. On the other hand, many of our "New England winter coughs" in elderly persons on close investigation turn out to be chronic phthisis and explain the incidence of tuberculosis in grandchildren and others in the family.

Again, the physician may declare the family history to be absolutely negative as far as tuberculosis is concerned, and fail to elicit the fact that a nurse or attendant who later died of consumption cared for the patient when a child.

The following definitions of family history and exposure emphasize these points:

> "Family History: An occasional case of tuberculosis in the patient's uncles, aunts, cousins, etc., should not be considered of importance. It is an important fact when the patient's immediate relatives, such as brothers, sisters, father, mother, or grandparents, have been tuberculous."
>
> "Exposure: Childhood exposure is of the greatest importance. Moderate exposure among normal, healthy adults of cleanly habits is of less importance. Of course, prolonged contact, with unhygienic habits or surroundings, may be a dangerous factor at any age."

DIAGNOSIS BASED ON SIGNS AND SYMPTOMS REFERRED TO THE CHEST OR LUNGS

CASE 7.—This patient, a woman of thirty, has been referred to me by a physician in another city because of persistent râles at the left apex. These were found on a routine examination, neither patient nor her physician suspecting the presence of tuberculosis. On careful inquiry I found that she has never been particularly strong or robust, but except for this and the presence of persistent râles I could discover very little else that was suggestive of tuberculosis either in the history or the physical examination. The râles have remained, however, on repeated examinations.

In this case the family and personal history were negative or nearly so. Constitutional signs and symptoms as defined above were not more marked than could be explained by nervous exhaustion and physical fatigue, but there was a slight—though very slight—cough, some sputum persistently negative, and definite, *persistent râles* at the left apex. On this evidence I am quite ready to make a definite diagnosis of incipient pulmonary tuberculosis.

CASE 8.—This young man is twenty-four years old, is over 6 feet in height, and weighs nearly 200 pounds; he comes to see me because he has been told that he has tuberculosis. His family and

his own history are practically negative. There is a slight cough, with some sputum. Physical examination shows dulness over the upper third of the right lung, with numerous crackling râles in front and back. These râles have persisted on several examinations.

This man is of the type that many physicians would at once dismiss from their office with the words, "Why, you are the picture of health! You simply can't have tuberculosis!" Nevertheless he does have tuberculosis, although his history does not suggest it and constitutional signs and symptoms are nearly absent. It is important to note that the persistent râles in this case and in the preceding one were at an apex and not at the base of the lung. Had the râles been at the base of the lung in either case I would have made an entirely different diagnosis. We have called attention to this in our diagnostic standards as follows:

> "Usually a process at the apices should be considered tuberculous, and a process at the base to be non-tuberculous, until the contrary is proved, excepting when a clear history of pleurisy is present."

The relationship of constitutional signs and symptoms to those in the lungs as illustrated in these cases is referred to as follows:

> "1. When constitutional signs and symptoms and definite past history are absent or nearly so, there should be demanded definite signs in the lungs, including persistent râles at one or both apices. By 'persistent' it is meant that the râles must be present after cough at two or more examinations, the patient having been under observation at least one month.
>
> "2. In the presence of constitutional signs and symptoms, such as loss of weight and strength, etc., as defined above, there should be demanded some abnormality in the lungs, but not necessarily râles."

DIAGNOSIS BASED ON PLEURISY WITH EFFUSION

CASE 9.—This young man, aged twenty-seven, apparently strong and robust, came to the clinic on account of increasing shortness of breath. He had a pain in the left side of his chest at first, which has since disappeared. There were evident signs of a large amount of fluid in the left pleural cavity. I sent him into the hospital at once, where his chest was tapped and 40

ounces of clear straw-colored fluid removed. A few râles were found at the right apex. Temperature and pulse are now normal. I have explained the exact situation to this man, that pleurisy is a mild form of tuberculosis, and that he must report to me every week for several months.

Until comparatively recently a case of pleurisy with effusion was treated purely as such, the fluid was drawn off if necessary, and little or no attention was paid to the tuberculous process that practically always lies in the background. It is not always easy to decide whether a patient with pleurisy with effusion should or should not be put under strict sanatorium régime. In my own cases I base my decision on the following points:

1. Whether or not there are constitutional signs and symptoms of a tuberculous toxemia, as defined above.

2. Whether or not there is any evidence of any intrapulmonary involvement at the apices or elsewhere.

At all events every case of pleurisy with effusion should be kept under observation for a few months at least, and the following statement concerning this in the diagnostic standards borne in mind:

> "One should consider a typical pleurisy with effusion as presumptive evidence of tuberculosis."

Likewise not only applicable to pleurisy with effusion but also to all of these cases is the following:

> "In every doubtful case one should demand that the patient be kept under observation for at least one month, with repeated sputum examinations, before a definite diagnosis is made."

AIDS TO DIAGNOSIS

Tuberculin Tests.—In children of fifteen years of age or under the von Pirquet cutaneous test is of great value in diagnosis, increasing in value as the age decreases. In adults it is of little or no significance. The subcutaneous tuberculin test should not be used except by those experienced in its use and thoroughly aware of its possible dangers. As a general rule I advise against its use in suspected cases of pulmonary tuberculosis. The com-

plement-fixation test is still in the experimental stage and is not yet available for general practitioners.

***x*-Ray.**—An *x*-ray examination *may be* of great value as an aid to diagnosis. I use the phrase "may be of great value" advisedly. There are many hyperenthusiastic roentgenologists who claim that the *x*-ray will reveal tuberculous disease earlier and more accurately than can be done by any other method. It is undoubtedly true that the *x*-ray will reveal certain changes and abnormalities in the lung that cannot be detected in other ways, but it must always be remembered that *x*-ray evidence is based on lights and shadows, and that in most instances active and recent processes cannot be differentiated from inactive and old processes. Furthermore, the value of the *x*-ray plate, be it ever so clear and distinct, is dependent on the man who interprets the plate. It is true that *x*-ray evidence interpreted by an expert who recognizes the limitations as well as the possibilities of this method of diagnosis is of great value, but it is still more important to remember that such evidence should never take the place of a careful and painstaking history of the patient and the study of his constitutional symptoms and local signs in the lungs.

DIFFERENTIAL DIAGNOSIS

Non-tuberculous Acute and Chronic Pulmonary Infections.—In Massachusetts during the past year there has been what has almost amounted to an epidemic of acute and subacute infections of the lungs, many of which closely resemble and have been called cases of tuberculosis. In some instances an exact diagnosis of such a condition can be reached only by waiting. In the majority of cases, however, careful study will show that tuberculosis is unlikely. The chief points of difference are as follows:

1. These non-tuberculous processes are usually at the base of the lung, whereas in tuberculosis the disease is usually at the apex.

2. Despite extensive signs in the lungs, constitutional symptoms, especially fever and rapid pulse, are often absent or very slight.

3. Although there often is a large amount of purulent sputum, repeated examinations for tubercle bacilli are negative.

4. The fact that extensive signs in the lungs gradually clear up or disappear in the course of a few weeks or months.

Such cases are often not only very difficult to diagnose but also very difficult to manage. One must always bear in mind that tuberculosis may be present despite negative evidence; also, and of still more importance, that it is unjust to go to the other extreme and stamp the patient as a consumptive, as I regret to say is often done, on insufficient evidence. Conservative, sound common sense is urgently needed in such cases as these.

Other Causes of Blood Spitting.—Our definition in the diagnostic standards states that "A hemorrhage of one or two teaspoonfuls of blood is presumptive evidence of tuberculosis." This is a safe rule. Occasionally, however, there occur frank hemorrhages that do not mean tuberculosis. Elderly persons with high blood-pressure and sclerotic arteries may raise considerable amounts of blood due to a ruptured blood-vessel in no way connected with a tuberculous process, although I admit that this would be very difficult to prove. Often in mitral stenosis and other forms of heart disease and occasionally in bronchiectasis and pulmonary cancer there may be real hemorrhages as defined above. These possibilities should be borne in mind.

Early hyperthyroidism, or exophthalmic goiter, often cannot be differentiated at first from early pulmonary tuberculosis. Fortunately, the treatment is the same, and time will usually give the correct diagnosis.

Malignant Diseases of the Lung.—Here again the differential diagnosis may be impossible at first, but also, as in hyperthyroidism, this question will eventually settle itself.

Pulmonary syphilis doubtless does exist, but it is certainly very rare. The fact that a person has a positive Wassermann and other evidence of a luetic infection along with certain abnormalities in the lung, and the fact that such abnormalities clear up under antiluetic treatment does not necessarily prove that the changes in the lung are due to syphilis, nor that the case is one of pulmonary syphilis. On the other hand, when luetic infection is known to be present in combination with marked signs in the lungs out of proportion to the constitutional signs and symptoms,

and when these clear up under antisyphilitic treatment, pulmonary syphilis must certainly be very seriously considered.

Other Causes of "Being Run-down."—In Massachusetts the medical profession and the public are both wide awake to the need of the early diagnosis of tuberculosis. The younger members of the medical profession, in fact, are so alive to this that anyone who loses weight or who becomes run-down from whatsoever cause runs a very serious chance of falling into the hands of some enthusiastic doctor who promptly labels him a consumptive. While this state of affairs is obviously better than the condition that existed ten years ago, when very few physicians made a definite diagnosis of phthisis until the disease was in the advanced stages and the sputum positive, nevertheless it is a condition that ought not to exist. Anyone who makes a positive diagnosis of tuberculosis without a positive sputum is taking on himself a very grave responsibility. We must remember that people will continue to get tired out, to lose weight and strength, to have colds that hang on, and to need vacations without being consumptives. Granted that certain of these conditions are due to latent tuberculous processes which are in danger of being roused to activity, in doubtful cases there is no need of telling the patient that he is a consumptive and that he must go to a sanatorium on such slight evidence as this. Here again common sense is the physician's most valuable asset in handling such problems.

Finally, I would emphasize these points as strongly as I can —namely, that the early diagnosis of pulmonary tuberculosis is no easy task; that it takes time, patience, and thoroughness to make a correct diagnosis; that the patient's happiness, health, and often his life depend on the advice given by the physician at this time; that the physician should realize the responsibility he is assuming in making his decision one way or the other; and, finally, that success in this field depends more on the use of common sense than on any other quality the physician may possess.

CLINIC OF DR. FRANKLIN W. WHITE

BOSTON CITY HOSPITAL

IMPROVEMENTS IN THE DIAGNOSIS OF CHRONIC ULCER OF THE STOMACH AND DUODENUM

Modern Methods of Examination of Patient; Importance of Location and Size; Use of the Stomach-tube and the Roentgen Ray; Desirability of Roentgen Evidence in Contradistinction to Roentgen Diagnosis; Necessity of Watching the Ulcer Itself and Its Effect on the Functions of the Stomach, etc.; Late Diagnosis of the Condition of the Ulcer During and After Treatment.

THERE have been great changes in the last few years in the diagnosis of chronic peptic ulcer. We have recognized the imperfections of some of our older methods of examination, and laid more emphasis on newer ones. We are now able to locate ulcers, to measure their size, and to study more completely their effect on the functions of the stomach. We are much better able to classify these ulcers in groups for treatment and to choose the treatment best suited to the individual case.

We are now able to follow the ulcers in a new way during their course of treatment, whether medical or surgical, and to see what becomes of them, whether they are getting larger or smaller, not depending wholly on what the patient tells us about his feelings, but *watching the ulcer itself* from time to time and its effect on the functions of the stomach, and changing our treatment to meet the needs of the individual case.

There are great advantages in this method by direct observation of the ulcer and the progress of healing by the Roentgen ray; it helps greatly in deciding for and against surgery. By directly observing the patient we can best protect him from the develop-

ment of cancer and make an actual, *early* diagnosis of secondary cancer and make a life-saving operation possible.

History.—I shall pass over rather briefly the use of symptoms in diagnosis, not because it is unimportant, far from it; but because there is little new. Most of the recent progress in the diagnosis of ulcer has been made by improving the methods of physical examination.

The most striking symptom, of course, is hyperacidity or "hunger-pain," which is present in more than four-fifths of the ulcers. The frequency of hyperacidity has tempted so great a surgeon as Moynihan to say that "hyperacidity is ulcer." This, of course, is not true, yet he did us a great service. In severe chronic "hunger-pain" we no longer make the diagnosis of simple hyperacidity and let the matter rest there; we look farther in every case to see if we can find an organic basis for this symptom, and in the severe persistent cases we usually do find an organic basis. This is a chronic ulcer in about two-thirds of the cases of severe hyperacidity and either a chronic appendix or a chronic gall-bladder in the other third.

The patients usually have the soda habit, and many vomit. The symptoms are usually intermittent, and show a special tendency to occur in the spring and fall.

In addition to proving the *presence* of a chronic ulcer, it is very important to know its *position*, whether in the stomach or duodenum, for we know that duodenal ulcers rarely become malignant, while gastric ulcers quite frequently do. If the ulcer is in the stomach we also wish to know whether it is near the pylorus or well up on the lesser curvature, for the first is much more likely to cause obstruction than the second.

It is a waste of time to try to locate the ulcer by the symptoms alone, and the reason is obvious. If we watch the stomach with the fluorsocope we find that the pylorus usually opens within a few minutes and food is discharged into the duodenum. In other words, within a short time after food is taken, an ulcer, whether in the stomach or in the duodenum, is equally bathed in food, the irritation of acid occurs just as promptly in one as the other; both are equally stirred up by peristaltic movement and spasm. It

is far more satisfactory to look directly at the ulcer with the Roentgen ray and *see where it is*, than to trust to symptoms to locate it.

The *size* of the ulcer is also very important in ulcer of the stomach, on account of the frequency of cancer changes in the large ulcers. We cannot judge of this by the history alone; frequently the symptoms are very severe in a small ulcer and may be very slight in a large one. This is well illustrated by the two following cases:

Fig. 135.—Good-sized annular defect at pylorus due to secondary spasm from small ulcer of posterior wall. (Case of Mrs. R. B.)

The first patient is Mrs. R. B., housewife, forty-five years of age. She has complained for two years of intermittent epigastric pain, with frequent vomiting, once of old food. The pain usually occurs one to three hours after meals. She has lost 20 pounds in weight. She has carious teeth, with pyorrhea. Abdominal examination shows finger-point tenderness 2 cm. below the xiphoid.

Test-meal showed normal secretion and a small twelve-hour residue. No blood in stomach contents or feces. *x*-Ray examination showed active peristalsis in the stomach, a good-sized residue up to twenty-four hours, with a moderate sized annular defect just above the pylorus (Fig. 135). Pain and vomiting improved but did not stop after ten days of medical treatment in

bed. The stomach emptied in eighteen hours under full doses of atropin. Operation was advised.

At operation a small ulcer with a crater 1 cm. in diameter was found on the posterior wall of the stomach about 4 cm. above the pylorus.

The following points are of special interest in this case: The symptoms were very severe and prolonged and yet the ulcer was scarcely more than 2 cm. in diameter. The ulcer was well above the pylorus and the long delay in emptying was due to spasm, not to organic obstruction. The large annular defect was due to secondary spasm from the ulcer, not to the ulcer itself. Even full doses of atropin only relaxed this spasm to a slight

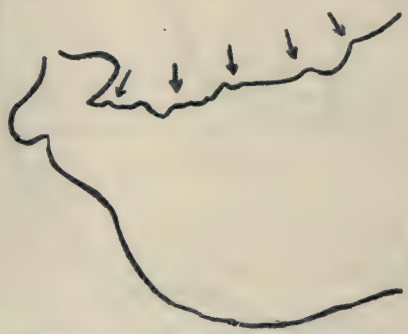


Fig. 136.—Long rigid irregularity of lesser curvature caused by large saddle ulcer. (Case of Mr. L. L.)

degree, and the improvement in emptying the stomach after atropin was only moderate.

This second patient, Mr. L. L., a Russian broom-maker, fifty-two years of age, complained of a slight cough for a few months. He had lost a little weight and had no digestive symptoms. A few days ago he "spit up" a little bright blood without nausea or cough. There was slight epigastric tenderness. *x*-Ray examination of the lungs showed increased density at both apices and a diagnosis of probable tuberculosis was made.

The stools showed a strong positive benzidin test for blood each time examined. This was the red flag of danger. We then made a systematic examination of the digestive tract and found that the

gastric secretion was very low, free HCl 5, total acidity 20. Blood was present. *x*-Ray examination showed a large six-hour residue and a rigid irregularity of the lower 10 cm. of the lesser curvature (Fig. 136). The diagnosis of large gastric ulcer with malignant changes was made.

In this case the digestive symptoms were so mild and unimportant that we almost made the mistake of not giving the digestive tract special study. Operation disclosed a large chronic, circular, saddle ulcer fully 12 cm. in diameter, with malignant changes.

With regard to *complications*, such as gross bleeding, the patient's history helps us. In order to count as a symptom the bleeding must be a real one, not merely a streak of blood, which is frequently found in any patient who has vomited repeatedly.

The presence of obstruction is often shown by the fact that symptoms which were intermittent become more or less continuous. The vomiting of old food is always important.

Acute perforation always gives us striking symptoms—pain, rigidity, collapse—while chronic perforation of ulcer, which, by the way, is twice as common as acute, gives no symptoms which can be distinguished from those of any chronic ulcer.

With regard to the development of cancer upon ulcer we must never wait for marked symptoms. We must get the text-book pictures of cancer entirely out of our head. If we wait for coffee-ground vomit, obstruction, lack of free HCl, palpable tumor, emaciation, etc., we have an absolutely hopeless case. In fact, I have heard that book of our great teacher, William Osler, on Abdominal Tumors called "a good autopsy manual" by a leading surgeon because it had so little clinical value.

The question is often raised whether cancer of the stomach is *ever* diagnosed early. A small cancer very rarely is unless it is just at the pylorus, as in Case 3.

In this third case a man of fifty years has had mild attacks of epigastric distress and vomiting for several years. General physical examination was practically negative. His gastric secretion was normal. No blood was found in stomach contents or feces.

There was, however, a small twelve-hour gastric residue and *x*-ray examination showed a very small annular defect at the pylorus with slight irregularity (Fig. 137).

On account of the obstruction unrelieved by medical treatment and the possibility of cancer (which was emphasized by the radiologist) operation was advised. A small annular scirrhous cancer was found at the pylorus which was successfully resected.

In this case the cancer, while very small, gave early symptoms because it was at the pylorus and caused definite obstruction.

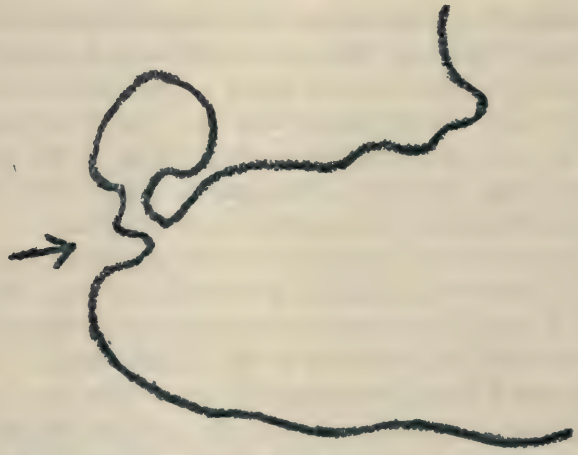


Fig. 137.—Small annular defect at pylorus due to small annular ulcer. Case 3 (from plate by Dr. A. W. George).

I want to emphasize, however, that *cancer on ulcer is and should be regularly diagnosed early*, not by the symptoms, but by the modern methods of examination which I will describe.

Physical Examination.—Since the valuable work of Rosenow and others we look much more carefully than ever before for sources of infection of an ulcer. We examine the teeth, tonsils, sinuses, appendix, and gall-bladder.

We note from statistics of operated cases that every third case of chronic ulcer has also an infected appendix and that every seventh case has an infected gall-bladder. If we examine the teeth carefully in ulcer cases we cannot fail to be impressed by the

large number of ulcer cases with infected roots. We must admit, however, that infected tooth roots are very common and great numbers of them are not associated with ulcer.

Modern diagnosis has shown that many of our older methods of examination were very imperfect. Let us briefly review some of these.

Take palpation—how little we feel in comparison with what we see with the Roentgen ray. In reviewing a large number of ulcer cases I find it is very rarely that I am able to palpate the ulcer. This is easily understood when we remember that the lesser curvature and the duodenum are the favorite sites with ulcer, and these are so frequently hidden under the edge of the ribs or liver that they are entirely out of reach when the patient lies on his back. Even tenderness is apt to be diffuse in the epigastrium, probably because we are not able to palpate very directly over the ulcer for the reason just given.

After having *seen* the ulcer with the Roentgen ray I have frequently returned to the patient in bed and absolutely failed to get any clear evidence of its presence by palpation.

Palpation of the erect patient before the fluorescent screen is another matter. If we see a deformed area and press directly over it, sharply localized tenderness has some value in diagnosing ulcer.

Percussion of the outline of the stomach is a method of very little value, which I have practically given up. If we percuss the stomach without inflating it the area of resonance is just about as likely to be the splenic flexure as the stomach, and if we percuss the stomach after moderate inflation with the patient on the back, we percuss the area of the gas-bubble which rises up under the abdominal wall in the middle of the stomach. In this position it gives us very little idea of actual outline. This is a very crude method and hardly worth the time it takes.

The *test of capacity* of the stomach, by pouring in liquid until the patient cries enough, is also of little value. The capacity of the stomach depends entirely upon the tone of its muscles. The normal stomach embraces its contents closely, no matter how small they are, and the amount which can be poured in without

discomfort depends almost entirely upon tone and sensitiveness, and varies greatly in different people with stomachs of the same size.

The *use of the stomach-tube* to test the secretion and emptying of the stomach has received a great set back since the free use of the Roentgen ray. I frequently see patients suspected of ulcer who have never been carefully examined except by the radiologist.

This is a mistake. There is no reason to give up the stomach-tube because we have the Roentgen ray. Tube tests are simple and cheap and give us valuable information. They are the only means of testing gastric secretion, and if secretion is either high or low we want to know it. They also tell us whether or not the stomach empties properly and about bleeding.

Tube tests have now taken their proper place, formerly considered very important, now always useful, but secondary.

The new Rehfuss tube, which is very small, like the Einhorn duodenal tube, is left in the stomach for several hours for the purpose of removing some of its contents for examination at intervals of fifteen or twenty minutes. The tube is so small that it is very easy to retain, and it has proved of very great value in studying the gastric physiology, but it cannot be considered a necessary diagnostic method in ulcer, and the frequently repeated examinations are not convenient outside a hospital or the office of a specialist.

Either the stomach-tube or the Roentgen ray can be used in deciding about the emptying time of the stomach. Twelve-hour residues are always important, and considerable six-hour residues call attention to the gastric function and require explanation. If we use the six-hour barium examination as a test of function we must allow no food in the interval. The radiologist is usually more interested in finding an actual lesion than in studying function, and is sometimes careless about the latter. I have seen several cases of ulcer in the last six months in which a report of good-sized six-hour residue was made and found that the patient took his barium meal at 10 A. M., took a hearty lunch at 1 P. M., and went for the six-hour examination at 4 P. M. The lunch held back some barium in the stomach and gave us a fictitious "six-

hour residue." This residue is a *minor* sign in ulcer, but as a test of function and guide to treatment it is valuable and should be carefully arranged. Fully two-thirds of the cases of chronic ulcer, whether of the stomach or duodenum, show some delay in emptying the stomach.

It is very important to decide whether this delay in emptying is due merely to spasm of the pylorus or to actual tissue narrowing. I want to emphasize here the use of atropin in deciding this question. Many a case of obstruction, which we believe at first to be organic, relaxes almost entirely under the use of atropin, and is shown to be merely the result of spasm. Dr. W. H. Mayo stated some years ago that delay in emptying the stomach in chronic ulcer is due to *actual tissue narrowing in less than 10 per cent. of the cases.*

This classification of the kind of obstruction is very important from the point of view of treatment. The cases with spastic delay frequently yield to medical treatment and are suitable medical cases. The cases with organic obstruction rarely yield to medical treatment and usually should go at once to the surgeon.

With regard to the use of atropin, we must not lay too much stress upon its use, for we find that full doses of atropin, even when continued for several days, do not always relax the spasm of an irritable stomach. The milder cases yield, the severer ones may not. In short, if a stomach relaxes and empties after the use of atropin we can conclude that the obstruction was due to spasm. If the obstruction does not relax after the use of atropin we have not absolutely ruled out spasm as a cause of delay. This point is well illustrated by Case 1 and also by this fourth patient. You note that I use only operated cases to prove my points, so we may be sure of our facts.

This fourth patient, Mrs. D. B., a woman of forty-six, has had indigestion for twenty-six years. Her husband had syphilis, and of her three children one was stillborn and two died within a few days. Her Wassermann reaction is negative.

She has complained of epigastric pain and vomiting about one hour after meals. This is always worse for ten days before and during the catamenia. In the last year she has been worse and

has lost 25 pounds. In the last two months vomiting has been persistent, with old food several times; no blood seen.

Test-meals showed normal secretion, blood present. *x*-Ray examination showed a deep incisura dividing the stomach into two equal parts (Fig. 138). The upper pouch emptied within five hours, the lower pouch was still full after twenty-four hours. The crater of a small ulcer was suggested in the lower pouch on the lesser curvature about halfway between the incisura and the pylorus. The pylorus was clear, smooth, and absolutely normal. With full doses of atropin the incisura did not relax and the lower pouch did not empty in twenty-four hours.

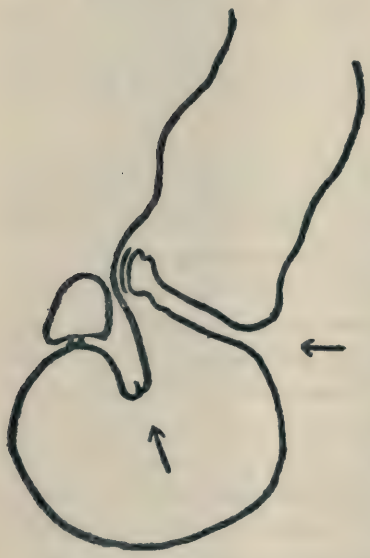


Fig. 138.—Hour-glass deformity from old healed ulcer, with small ulcer with slit-like crater lower down on lesser curvature. (Case of Mrs. D. B.)

We could not decide whether the hour-glass contraction was organic or spastic. We decided that the pylorus was normal, but was kept shut even for as long as twenty-four hours by severe reflex spasm from the small ulcer in the lower pouch.

Operation was advised and a true hour-glass stomach was found resulting from scar tissue and adhesions of an old ulcer in the middle of the lesser curvature. An ulcer 3 cm. in diameter was found halfway between the hour-glass contraction and the pylorus, the latter was normal.

The upper and lower pouches were connected by a wide gastrogastrostomy, the ulcer in the lower pouch destroyed with the cautery, and a gastro-enterostomy done. The patient made a perfect recovery and now is practically free from symptoms.

This case shows how difficult it may be to decide whether an hour-glass contraction is organic or spastic, and also how long a

normal pylorus can be kept closed by spasm from an ulcer some distance above it, and also how difficult it is sometimes to relax the spasm with atropin.

It is an interesting example of the intimate knowledge we can now get of all parts of the stomach and their workings by the combination of functional tests and the study of the living anatomy and physiology with the Roentgen ray.

Another important point—muscular spasm is a very variable, intermittent affair, and a patient with spasm of the pylorus does not always behave alike at different times, entirely apart from the use of drugs, and in deciding questions about treatment or operation on such a case more than one examination may be needed.

This fifth case, Mr. M. L., a clerk of twenty-four, suffered with hyperacidity for eight years, and nine months ago had several hemorrhages from the stomach, and after two weeks of medical treatment, in which bleeding continued, a gastro-enterostomy was done. His diet since operation has been careless at times and intermittent hyperacidity continued with rare vomiting. He gained 30 pounds since operation.

A week ago an *x*-ray examination, at another hospital, showed active peristalsis, the greater part of the food passed through the pylorus and only a little through the new opening. There was a medium-sized six-hour residue. Because of the persistent symptoms—hyperperistalsis, gastric stasis, and small passage of food through the stoma—a diagnosis was made of partial closure of the new opening and a second operation advised. The patient objected to this and came to us for examination.

On two separate occasions the stomach emptied rapidly, leaving no residue in five or six hours. We saw no ground for operation and the patient has been entirely free from symptoms for months with more careful diet and medical treatment. We can only explain the difference in the action of the stomach on the several occasions by the variable amount of pyloric spasm. It is not always safe to make an important decision after a single examination of the stomach.

The effect of ulcer deformity on the emptying of the stomach is a very interesting question. We find with the Roentgen ray

that the oldest ulcers, as a rule, show the most deformity, but they do not necessarily show the most obstruction. Deformity means old scar tissue or adhesions as well as active ulcer which may cause much deformity from spasm. Case 1 (Fig. 135) is a good example of a small ulcer with much obstruction and Fig. 139 shows a duodenal ulcer with a great deal of deformity but no obstruction at all.

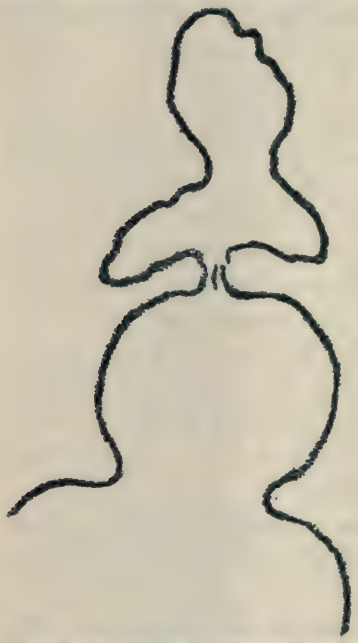


Fig. 139.—Marked deformity of duodenal cap with no obstruction.

Tests for blood we will pass over briefly, as they are well known. A test for blood in the feces on a meat-free diet in the absence of piles is a red flag and shows something is wrong. Blood in the stomach contents with delicate tests, such as guaiac or benzidin, is much less important, as it comes frequently from the slight rubbing of the tube. Personally I much prefer the benzidin to the guaiac test on account of its somewhat greater delicacy and easier technic. I will give the best technic of the old benzidin test. I see it so variously done and its delicacy depends so much on technic.[1] One of the best ways of testing

[1] The material for examination consists of simple gastric contents; or of a pea-sized piece of feces thoroughly stirred in a test-tube into about 4 c.c. of water. This is brought to a boil to destroy oxidizing ferments. Ten drops of a fresh solution of benzidin (prepared by shaking a knife-tip of benzidin in about 2 c.c. of glacial acetic acid) is added to 3 c.c. of a 3 per cent. (ordinary commercial solution) of hydrogen peroxid in a test-tube. This mixture serves as a control of the cleanliness of reagents and glassware.

To make the test, add 2 or 3 drops of the boiled gastric contents or of the feces mixture to the peroxid-benzidin mixture without shaking. A clean green or blue ring appears within a minute or two when blood is present.

It is best to use only pure reagent of best quality and to avoid peroxid solutions containing acetanilid as a preservative. I use dioxygen. The glassware must be scrupulously clean.

feces is to smear a thin layer on a clean slide with a glass rod or match and pour a few drops of the benzidin-peroxid mixture on it.

The simplest blood test for the practitioner are the *benzidin tablets* of Dudley Roberts, put up by Squibb & Sons. One tablet is placed in a clean saucer with enough stomach contents to wet the tablet thoroughly, but not to cover it. Then a drop or two of glacial acetic acid is dropped upon the tablet; if blood is present the tablet turns greenish blue. The same test can be used with feces, thinned with a little water.

Blood tests should not be relied on to *diagnose* ulcer, since we only get a positive result in about one-third of the cases. They do help us to judge the activity of an ulcer and also to rule out cancer. The latter is far more likely to give a positive test and give it constantly.

The *Einhorn string test* I consider a thing of the past. It has little value. I have given it a thorough trial and have given up using it. The results are difficult to interpret. Smithies found it positive in only 7 cases out of 318 gastric ulcers which were verified by operation.

We do a *Wassermann reaction* as a routine on ulcer cases. The results show that syphilis is a rare cause or associate of ulcer. A positive reaction was found in less than $\frac{1}{2}$ of 1 per cent. of a series of about 200 private cases of ulcer and in less than 2 per cent. of about 200 hospital cases of ulcer. This figure is distinctly less than the percentage of syphilis in total hospital cases, which is at least 4 or 5.

The **Roentgen ray** is our newest and greatest addition to the methods of diagnosing ulcer, and it sometimes seems as if it were worth more than all the other methods put together, but this is hardly true; as a matter of fact, and if patients are carefully studied the diagnosis is made in four-fifths of the cases of chronic ulcer before the *x*-ray examination is begun.

The Roentgen ray, however, does help us immensely, not only in deciding whether an ulcer is present or absent but also where the ulcer is, and how large it is. These questions are very important, as I have already said. The Roentgen ray also helps

greatly in diagnosing doubtful gall-bladder and appendix cases which simulate ulcer.

With the discovery of the great value of Roentgen examination in ulcer a bad practice is growing of sending poorly studied digestive cases to the radiologist and accepting his word as final. Let me warn you against an "*x*-ray diagnosis" of any gastro-intestinal lesion.

Twenty-five years ago at Harvard I was taught to make a complete genito-urinary diagnosis from a bottle of urine. We do not do that any more. We want the patient, his history, his other physical signs, as well as the urine to give us our diagnosis. A sputum loaded with tubercle bacilli may be enough to settle a case, just as the deep ulcer crater in the lesser curvature with deep incisura or the constant marked clover-leaf deformity of the duodenum usually is distinctive of ulcer; still we do well to take the Roentgen examination as Roentgen evidence and put it with the other clinical evidence in making a diagnosis. I have seen dreadful mistakes made from one end of the gastro-intestinal tract to the other from disregard of this rule. I have seen cancer of the esophagus diagnosed by a leading radiologist when a second year medical student could have made the correct diagnosis of cardiospasm from the history of *dysphagia of ten years' duration without loss of weight* in a very nervous man. I have seen a diagnosis made by an expert of a gall-bladder packed full of stones, when at operation (incidentally fatal) no disease of the gall-bladder was found. I have seen a report of an entirely normal colon made by another leading radiologist in a man constantly passing pus and blood, and a second examination reveal a cancer of the sigmoid previously hidden by a loop of bowel.

We want Roentgen evidence, not a Roentgen diagnosis. Not all Roentgen evidence is alike; some is very slight and dubious, some very strong, like, for example, the difference between palpating a large irregular abdominal tumor in a thin patient and feeling a vague resistance in a fat one. The profession is not yet educated to recognize these differences in Roentgen evidence. We must remember that the radiologist, like every other consultant, often faces a disagreeable dilemma. He naturally wishes to

make his diagnosis as definite as possible, but the evidence is often doubtful.

This is not the place to discuss the technical details of Roentgen-ray examinations. I will merely say that in chronic ulcer the tendency is to base our diagnosis less on so-called indirect signs, such as changes in peristalsis, spasm, and six-hour residue, and lay most stress on the actual demonstration of the ulcer itself by finding a defect in the stomach or duodenal wall. The indirect signs are valuable. They serve as a red flag and call our attention to the fact that something is wrong with the stomach which requires explanation, but they appear in ulcer *and in other conditions also* which cause reflex irritation and spasm of the stomach, such as chronic appendix or gall-bladder or a general condition of nervous irritability.

There is probably not a place in the digestive tract where Roentgen signs are so definite as in the duodenum; not in the stomach or in any other part of the bowel. This is because the lesions are found in the first inch or so of the duodenum, and we can concentrate our attention on a very small area. Where the best technic is used, definite evidence of duodenal ulcer is found in 90 per cent. or more of the severe chronic cases which come to operation. In the milder cases this percentage is not so high, and we have some difficulty in distinguishing ulcer from adhesions.

The chronic indurated ulcer of the stomach along the lesser curvature or near the pylorus is usually found with ease with the Roentgen ray. This is very important. *This is our opportunity to prevent cancer* by discovering the *location* and *size* of the ulcer. Size is very important, for MacCarty has shown that more than half of the ulcers of the stomach, with a crater as large as a quarter, are becoming malignant. We very rarely discover an early *primary* cancer, but we can discover and locate the good-sized gastric ulcers and get them to the surgeon in time to prevent the spread of hopeless cancer.

Let me explain this so there may be no mistake. We cannot look at an ulcer with the Roentgen ray and tell by its *anatomy alone* whether it is cancerous or not. These microscopic changes in the cells of the ulcer do not show on *x*-ray plates. If any one

has any lingering doubts on the matter let him read MacCarty's paper on "The Pathological Reasons for the Legitimate Error in *x*-Ray Diagnosis of Gastric Carcinoma and Ulcer."[1]

The important point is not anatomy, but *location* and *size*.

It is said that the soft, freshly bleeding ulcer is often missed on *x*-ray examination, and also that ulcers of the posterior wall may be easily overlooked because we cannot get them in profile. They are hidden behind the mass of material in the stomach in front of them.

I do not know what to say about the soft, freshly bleeding ulcer, because Roentgen examinations are usually not made in such cases at the active stage, but with regard to ulcers of the posterior wall I do not think they are very often overlooked. By examining the stomach in various oblique positions we get almost every side of the stomach in profile, and, in addition, an ulcer of the stomach, wherever placed, usually causes irritation and spasm of the circular fibers of the stomach, and we have a telltale spasm or incisura just at the level of the ulcer. Case 1 is an example of this. There was a very large circular spasm near the pylorus, and instead of finding a large ulcer at operation, as might be expected, we found a very small ulcer of the posterior wall. In addition, if we watch the stomach fill, with ulcer of the posterior wall, the filling is often irregular, a little puddle of barium collects near the ulcer, which later is covered up. Pyloric spasm and delay in emptying is naturally just as common with posterior ulcers as with any others, and by a combination of all these signs they are usually found. It is harder to judge their size than those of the lesser curvature and it is harder to follow the results of treatment by looking at them.

Statistics about the frequency with which chronic ulcer is found have not much value. They apply only to the more severe cases, with marked deformity, which are readily found, and which are much more likely to come to operation than the doubtful ones. There is no question that the Roentgen-ray examination almost always detects marked cases of chronic ulcer, "the surgical clinic cases," and, as a matter of fact, does a good deal more than

[1] American Journal of Roentgenology, February, 1917.

this. We can distinguish quite a variety of anatomic and functional types of ulcer with the Roentgen ray. The ulcer may be high or low, small, bitten out, or large and rigid, or deeply perforating, or with hour-glass deformity, or obstructive. We may have several types of peristalsis or spasm or incisura.

Several of these are illustrated by Figs. 142 to 146. A few tracings of the normal duodenum are shown for comparison (Figs. 140 and 141).

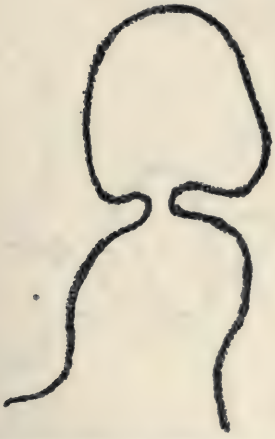


Fig. 140.—Normal duodenal cap (life size).

Fig. 141.—Normal duodenal cap (life size).

The Roentgen ray can also be used to great advantage, as I shall show at another time, in judging the results of either medical or surgical treatment, by detecting the anatomic changes which have occurred in the course of healing and in showing the changes which have occurred in peristalsis and in the emptying of the stomach. These changes in motor function can, of course, be readily detected by the use of the stomach-tube after an appropriate meal, and this method, so simple and easily applied, should be freely used for this purpose by the general practitioner. On the other hand, a single glance with the fluoroscope five or six hours after a barium meal gives us similar information without the necessity of troubling the patient or the stomach with

the tube, and is very convenient where the Roentgen ray is available.

This *late diagnosis* of the condition of ulcer after treatment I consider very important, so much so that I repeat some of the functional tests after two or three weeks of treatment, and also ask all cases to report for examination at least once in three months for the first year after treatment whether symptoms are present or not. I make a general physical examination, test the stools for blood, estimate the motility of the stomach with a barium meal, and make a direct examination of the ulcer with the Roentgen ray, using the fluoroscope or plates.

Fig. 142.—Ulcer crater in middle of lesser curvature with incisura opposite.

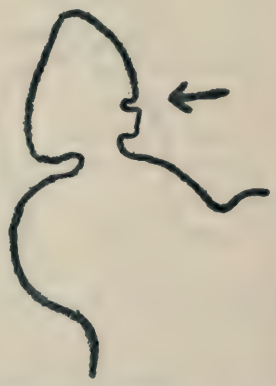


Fig. 143.—Deformity of cap due to duodenal ulcer (life size).

This kind of examination helps us, above all, to *individualize the treatment.* All ulcer cases can no more take the same treatment than all diabetics can eat the same diet. We treat ulcer according to its position and size and the changes in function which go with it. The treatment is an experiment to be watched and followed, like increasing the diet in a diabetic.

I want especially to emphasize the *need of a good follow-up system* in chronic ulcer. This is just as necessary as in diabetes. These ulcers are essentially chronic. This should be carefully

explained to the patient. The greatest failure I see in medical treatment is the lack of following the cases carefully for months and protecting the stomach from irritation for a long time.

There is no such thing as "the ulcer treatment" any more than "the diabetic diet." We do not want to lose track of a case of diabetes and only have him report when there is sugar in the urine, neither do we wish to lose track of a chronic ulcer and only have him report when his symptoms recur. To watch the patient with chronic ulcer and protect him from recurrence is just as much our business as to keep the diabetic sugar free.

Fig. 144.—Deformity of cap due to duodenal ulcer (life size).

Fig. 145.—Deformity of cap due to duodenal ulcer (life size).

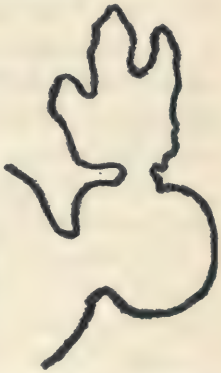


Fig. 146.—Deformity of cap due to duodenal ulcer (life size).

This observation of the patient has great value in protecting him from cancer. It is safe to say that in nine-tenths of the ulcers which "go bad," cancer could be avoided by an efficient follow-up system and constant weeding out of cases unsuitable for medical treatment.

It is interesting to note that while we have seen the deformity of *gastric* ulcer entirely disappear in a number of cases after medical treatment, thus far we have not seen a single markedly deformed duodenal cap which has filled out to its former smooth plump contour after treatment. This is true even in cases which have remained entirely without symptoms for a year or more and which we consider cured. The deformity of the duodenum has greatly lessened, but *not entirely disappeared.* Evidently a

certain amount of scar tissue or adhesions have persisted which still deform the delicate wall of the duodenum.

The things which I especially wish to emphasize in this clinic are as follows:

Some of our older methods of examination of the stomach in ulcer, such as palpation, percussion of outlines, and string tests, are very imperfect. We must not rely on them, but use better ones.

The stomach-tube should not be given up simply because we have the Roentgen ray; use both, they supplement each other.

Tests for blood have more value in showing the activity of an ulcer and in ruling out cancer than in diagnosis of ulcer.

A pure "Roentgen diagnosis" of ulcer or any other gastro-intestinal lesion is undesirable. Examine the *patient* as well as the plates. Roentgen evidence is not all alike, some is strong, some is weak.

Value of the Roentgen examination in chronic ulcer, not only to detect the ulcer, but to locate it and measure its size.

The importance of knowing where the ulcer is and how large it is in making an *early* diagnosis of cancer developing on ulcer, and thus protecting the patient.

Obstruction of the pylorus is usually due to secondary spasm from ulcer, not to actual obstruction by ulcer tissue or adhesions.

The use of atropin in deciding which stomachs with ulcer can be made to empty and which cannot. The classification of the kind and degree of obstruction is very important in choosing medical or surgical treatment.

The variability of spasm of the pylorus, and the necessity of more than one examination of the stomach in deciding important questions about gastric motility and its treatment.

The aid of the Roentgen ray in making a *late diagnosis* of the condition of ulcer during and at intervals after treatment, by direct observation of the anatomic and functional changes, which take place in the stomach and in the ulcer. A good follow-up system is just as necessary in chronic ulcer as in diabetes.

The deformity in gastric ulcer often disappears entirely after treatment. In duodenal ulcer this is evidently much less common.

CLINIC OF DR. K. H. THOMA

ROBERT BRECK BRIGHAM HOSPITAL

THE RELATION OF THE TEETH AND JAWS TO GENERAL MEDICINE

The Interrelation of Oral Infections and Somatic Diseases. The Effects of Infection. Bacteria and Bacterial Poisons. Frequency and Pathology of Oral Infections. Subperiosteal and Subgingival Abscesses. Dental Granulomata. Cysts. Pus Pockets and Pyorrhœa Alveolaris. The Mode of Distribution of the Infection in Oral Focal Disease. The Importance of Always Investigating the Mouth.

SUPPURATIVE processes of the jaws due to diseases of the teeth have occurred in all periods of history. The Greek historian Herodotus, who went to the shores of the Nile to learn the sacred mysteries and sciences of the Egyptians, found that surgery and medicine were divided into distinct professions and that among these specialists there were surgico-physicians who treated the diseases of the teeth. Tooth abscess must have been a very common trouble in the Predynastic Egyptian period as well as in the Old and Middle Empires, and apparently it was not known at that time that the extraction of the tooth would have speedily cured the trouble. I was fortunate in being able to examine a group of ancient Egyptian crania of those periods at the Peabody Museum of Harvard University, which date back to the year 4800 B. C. Among them I found a large number showing destruction of bone due to alveolar abscesses which was extensive in many cases.[1] If we continue our studies of anthropology we find in the writings of Hippocrates, who was born 460 B. C., the

first observation of systemic effects due to dental disease. He says that at the approach of dentition pruritus of the gums ("gingivarum exulcerationes") occurs, and fever, convulsions, and diarrhea, especially when cutting the canine teeth. The period of dentition was apparently accompanied by a great deal of trouble in those times and was probably frequently complicated by infection. In our more recent literature we find many cases of septicemia and pyemia originating from mandibular or maxillary infection, and no one today will dispute the fact that in the oral cavity you may have conditions present from which acute general infection can result. The discovery that an infectious focus may be the source of entirely different conditions than those observed in acute general sepsis has only recently been recognized. Careful clinical observation, extensive research work, and animal experiments have shown that a large number of local and general diseases are due to an infectious focus in some remote part of the body. This, in turn, has opened up a new field to researchers in oral surgery and has revolutionized diagnosis and treatment of dental and oral diseases.

I shall not endeavor to discuss the theory of focal infections. It may, however, not be amiss to say that the focus must not necessarily be in an acute condition; it is rather more frequently a chronic lesion which is quite often disregarded by the patient and physician because it may not give any local discomfort, and unless it is on the surface its site can only be located after the most careful examination by well-trained specialists.

The Site of the Focus.—The most frequent location of the focus of infection is in the head, and especially in the nose and accessory sinuses, the throat, the mastoid process, and the oral cavity. The gastro-intestinal tract with the vermiform appendix and the gall-bladder, as well as the genito-urinary tract, are other fields in which we often find primary lesions which cause systemic disease. It is not in the scope of this paper to describe all the diseased conditions which lead to secondary involvement of other parts of the body, and I shall, therefore, confine myself to the diseases of the mouth and teeth, their relation to local and general diseases and their clinical manifestations.

The Interrelation of Oral Infections and Somatic Diseases.—Dentists have discovered long ago that during the developmental stage of the teeth general diseases may produce lesions in the tooth germs. Scarlet fever, measles, and congenital syphilis may be the cause of permanent defects of the enamel, easily recognizable in the erupted teeth. In tuberculosis, typhoid fever, and syphilis we frequently find secondary lesions in the mouth. That the reverse condition is possible is a logical conclusion. It has been borne out further by observation of cause and effect, by animal

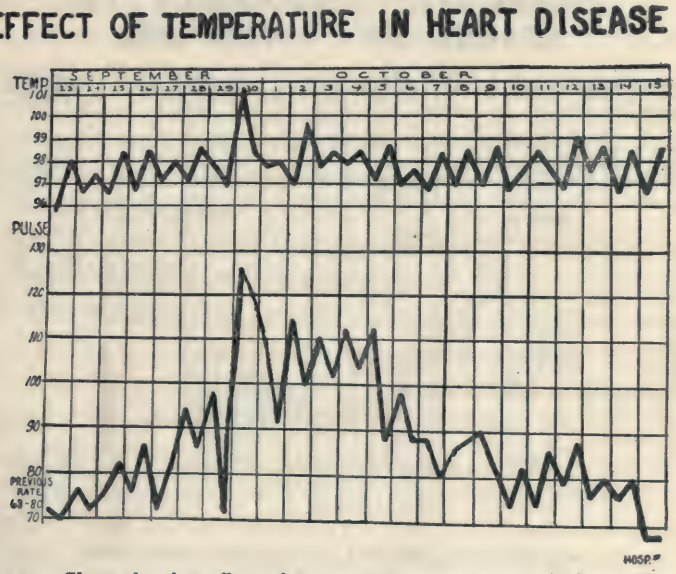


Fig. 147.—Chart showing effect of temperature on pulse-rate in heart disease.

experimentation such as undertaken by Hartzell and Henrici,[2] by bacterial studies in finding the same bacterium in the focus and secondary lesion, and still further by carefully following up the effect upon the general health and secondary lesion from eliminating the focus. In connection with this we must bear in mind that we may get an improvement as an indirect result by improving the general health of the patient.

Effect of Infection.—Through the courtesy of Dr. McCrudden, of the Robert Breck Brigham Hospital, I take pleasure in re-

producing some of the charts he has made in connection with his studies of infections.

The *first chart* (Fig. 147) shows the effect of temperature in heart disease. The patient, Hospital case No. 239, had a past history of measles and scarlet fever when a child, had first signs of heart trouble eight years ago, used to get somewhat short of breath, but has been fairly well up to three years ago; has recently had attacks of heart trouble with dyspnea and slight swell-

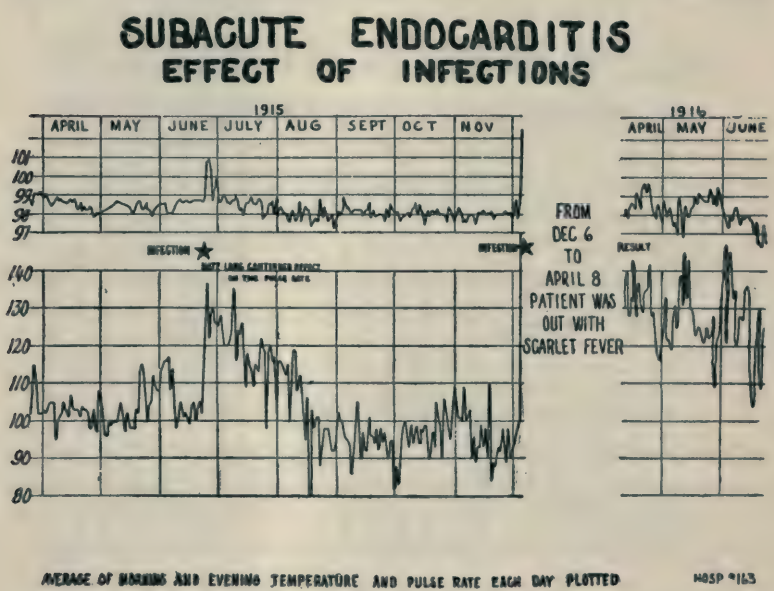


Fig. 148.—Chart showing the long-continued effect of an infection on the pulse-rate.

ing of feet and ankles. Diagnosis was made of aortic regurgitation and double mitral. September 30th a slight infection occurred which is indicated by a rise of temperature to 101.4° F. and to 99.8° F. on October 2d. The effect this had on the heart is indicated by the pulse-rate which remained between 90 and 125 for several days.

The *second chart* (Fig. 148) shows the effect of an infection in a case of endocarditis. The patient, Hospital case No. 163, a child three years old, had the following past history: Began to

walk at one year of age, German measles and pertussis at one year, sore throats at different times and fever, but cannot remember just when. Examination reveals a systolic murmur heard in mitral area, in axilla, and left back, presystolic roll and thrill at apex, diastolic murmur heard over aortic area and transmitted downward. She was admitted to hospital March 25th; temperature was below 99° F., and pulse between 100 and 110 until June 24th, when an infection occurred which is indicated in the temperature curve by a rise for a few days (note the long-continued effect on the pulse-rate which lasted until August 15th). A very serious infection occurred in December when the patient contracted scarlet fever and was away from the hospital from December 6th to April 10th. The serious and long-continued effect this had on the heart is shown on the right-hand side of the chart. Note that the pulse-rate remained between 120 and 145 for three months more, up to June 22d, when she died.

The *third chart* (Fig. 149) I compiled from two of Dr. McCrudden's charts. It shows the effect of a vaccine on the strong heart (of Hospital case No. 225) and on the weak heart (Hospital case No. 211). The former was a patient fifty years old, suffering from chronic arthritis, and had the following past history: Had measles and scarlet fever when six years old. Her present illness started a year ago last May (twenty-one months ago), when she began to notice a pain in the ball of the left foot. Soon after this the ankle and the shoulders became lame and painful. The foot was swollen at the time, but more particularly at night. The wrist and knees next became involved. In December she was obliged to give up work altogether and has been bed-ridden ever since. She was a well-developed and well-nourished woman, lungs normal, heart sounds regular and of good quality, no thrills were palpable, no cyanosis or edema. Otherwise normal except for the loss of function in the shoulders and deformity of the left wrist. She was admitted February 3d. February 20th vaccine treatment was begun. Injection made at 3.30 P. M. into median basilic vein of right arm of 75,000,000 typhoid bacteria with 100 c.c. of normal salt solution. She had a definite chill which lasted twenty minutes, but otherwise no heart symptoms. Temperature

and pulse curve show on chart, and by 9.30 P. M. these were normal. Patient said she had the most restful night she had had for a long time. February 28th vaccine, 100,000,000 bacteria, injected into right arm at 4 P. M. At 4.45 P. M. a severe chill occurred, lasting about twenty minutes. Temperature curve as shown on chart was normal again at 9.45 P. M.

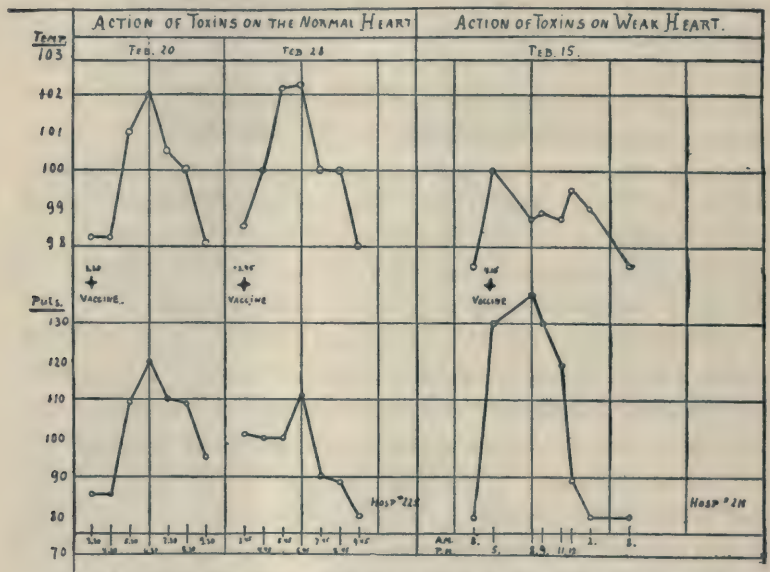


Fig. 149.—The first two curves show the effect of a toxin on the normal heart. Note the effect on the pulse. There were no heart symptoms. The third curve shows the action of the same toxin on a weak heart. Note the pulse curve. From 5 P. M. until the next day there were marked cardiac symptoms, dypsnea, cyanosis, coughing, headache, salmon-colored sputum, and tenderness over precordia .

The second patient, Hospital case No. 211, a woman thirty-six years old, was admitted for chronic arthritis. The following is her past history: Measles and diphtheria and scarlet fever when a child. At age of twelve years had "Saint Vitus dance" which lasted two years. Had two attacks of pneumonia when fifteen years of age; rheumatic fever seven years ago, short attack, one month, febrile, all joints, no after-effects in joints, no subsequent acute attack, no tonsillitis. Present illness began eighteen months ago, when she noticed pain and stiffness of the

left knee which was soon followed by an involvement of the right knee. A year later the left elbow began to trouble her, followed by similar involvement of the right elbow. Six months ago was troubled with pain and swelling in the joints and fingers of both hands. Appetite good; no digestive discomfort; no coughing or expectorating; no dyspnea, does not complain of shortness of breath or palpitation; has had some edema in ankles; no headache. The following is the report of the examination: Present examination: recumbent, slight edema of both ankles, teeth poor, glandular enlargement in submaxillary region on both sides; heart—apex-beat not visible, apex-impulse felt in fifth interspace, mid-clavicular line, base on level with third rib, apex in fifth interspace, right border $3\frac{1}{2}$ cm. from midsternal line; left border 11 cm. from midsternal line, P_2 greater than A_1.

While there was no evidence of physiologic heart disease, a systolic murmur was found. When admitted October 9th she complained of pain in joints, trouble with right hip and elbows, but generally was in good condition. February 15th vaccine administered, 75,000,000 bacteria intravenously at 4.15 P. M. At 5 P. M. patient showed signs of reaction—chill, typical spasmodic shaking, but no complaint of cold; had marked cardiac symptoms at 9 P. M., patient was dyspneic and cyanotic and coughing. Sputum was salmon colored. Distress, dyspnea, and headache lasted until about midnight. Next day there was tenderness and palpitation over the precordia.

These 2 cases therefore illustrate that a patient with a strong heart can take care of a slight infection such as a vaccine, while the other patient, who had no physiologic heart disease but whose heart was weak, developed from a small infection such as the administration of the same vaccine most severe heart distress.

The *fourth chart* (Fig. 150) shows the improvement which resulted in a case of endocarditis through the removal of two teeth with chronic abscesses. The patient, Hospital case No. 116, age thirteen, had measles when very young and scarlet fever seven years ago. He had never had any sore throat. Seven years ago he started to have pain in the joints, mostly in the shoulder region, associated with fever. Shortly afterward he

complained of pain over the precordia and of dyspnea upon exertion. He was kept in bed except for meals. Physical examination showed lungs negative, heart-apex visible and palpable in fifth interspace, 11 cm. from the midsterum. Over the apex was felt a distinct presystolic thrill; sounds were of fair quality, but rapid, at mitral area is heard a presystolic murmur; over aortic area is a diastolic murmur and over pulmonic area is a systolic murmur. Patient was admitted to the hospital November 6th; temperature 100.6° F., pulse 140, respirations 28, blood-

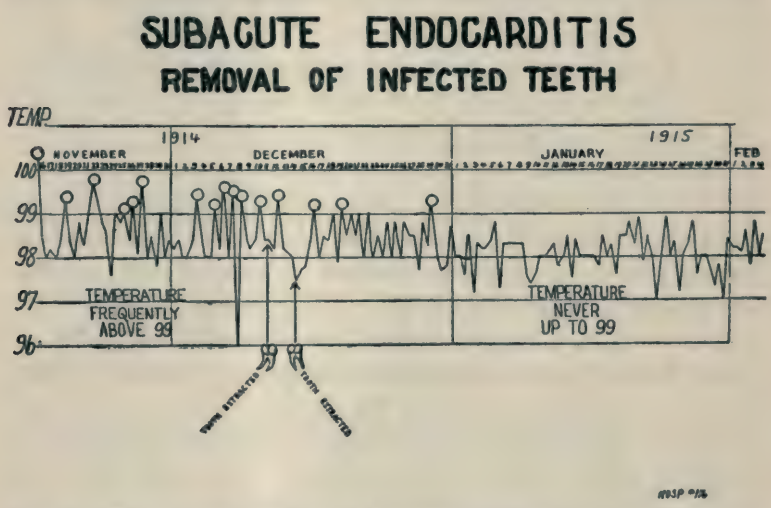


Fig. 150.—Chart showing the effect of the removal of infected teeth on the temperature curve in subacute endocarditis.

pressure $\frac{125}{80}$. He was put on a light diet and kept in bed. *x*-Rays taken of his teeth showed abscesses at the roots of two lower first molars. I extracted the first on December 11th and the other on December 14th, and after this the temperature was only three more times over 99° F. in December, and in January it was never up to 99° F. From the time he was admitted until the time he received dental treatment, December 11th, the temperature was quite frequently above 99° F., as indicated by the red circles.

The *fifth chart* (Fig. 151) shows, besides temperature and pulse, a weight curve indicating the effect of infection upon nutrition.

The patient, Hospital case No. 76, is a case of subacute endocarditis in a girl aged sixteen. She had measles and whooping-cough in childhood, rheumatic fever three times, the first time when a child, the second time one year ago, the third time in March or April. Two months ago operation for appendicitis; after discharge from hospital following operation was taken with German measles and rheumatism and was in hospital for three weeks. Left hospital on a Thursday, and on the following

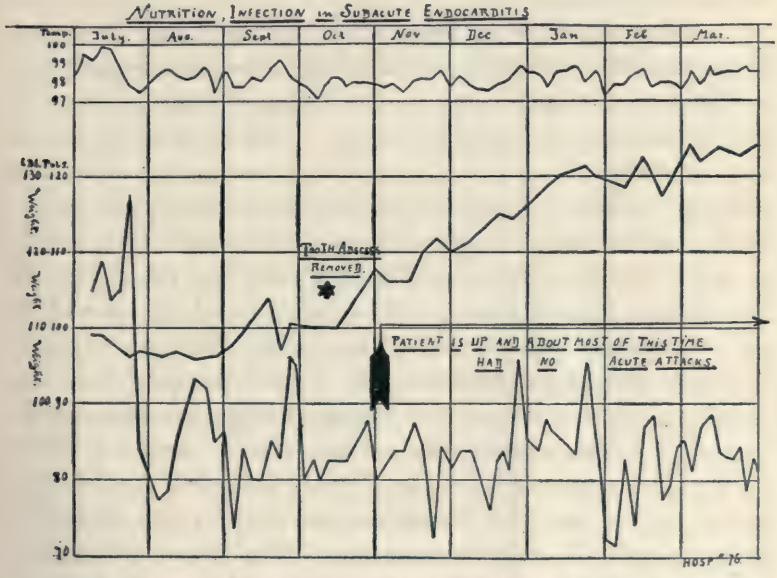


Fig. 151.—Chart showing temperature and pulse plotted over three days. Note the increase in weight, as demonstrated by the middle curve after the removal of a tooth abscess. The patient was up and about most of the time and had no acute attacks after the middle of October.

Tuesday felt weak and became unconscious. Following this came rheumatism, beginning in hands (joints), wrist, left shoulder, and neck; pain across upper part of chest. Examination shows a well-developed and fairly well-nourished girl, color pale, lungs normal, heart action rapid but regular, presystolic thrill palpable over the apex, loud blowing presystolic and systolic murmurs loudest over apex and transmitted outward; also diastolic murmur. Patient admitted July 5th, received

house diet for a short time at first, later milk, bread, and fruit. The treatment was principally quiet, rest, full diet, and digitalis. She had complained of a "sinking feeling" quite frequently at first, but later only occasionally. October 12th had left bicuspid extracted, *x*-ray of which showed abscessed root. After this she improved noticeably, and since November has been up and about most of the time without acute attacks. Her weight has increased from 110 to about 130 pounds in the last few months, as shown in the curve of the chart.

Bacteria and Bacterial Poisons.—The mouth is an ideal place for bacterial life, and an unclean mouth or one containing diseased conditions may harbor any number and variety of fungi, yeast, pathogenic and saprophytic bacteria. The most infectious lesions of the mouth may be caused by any of a large number of pyogenic bacteria, and secondary invasions of saprophytes is rather the rule than the exception. The latter live upon the products of decomposition and have a great deal to do with the formation of gases, the odor of the exudates, and the color of the pus. Originally the bacteria of the mouth were studied with the idea of finding one of them to be the etiologic factor of a definite lesion, but no one has been able to demonstrate specific organisms in the various diseased conditions. Any one of the pyogenic bacteria may cause an alveolar abscess or a pus pocket at the gingival margin. We almost always find a mixed infection with a great variety of combinations. The following list gives the bacteria which are most commonly found in oral lesions:

Streptococcus hemolyticus (often found in acute abscesses).
Streptococcus viridans (very common in blind abscesses).
Staphylococcus aureus.
Staphylococcus albus.
Diplococcus pneumoniæ.
Diplococcus of Connellan-King.
Bacillus typhosus.
Bacillus tuberculosis.
Bacillus mesentericus.
Bacillus tetragenus.
Bacillus pseudodiphtheriæ.

Bacillus fusiformis,
Bacillus bifidus communis,
Bacillus ramosus,
Bacillus perfringens,
} anaërobic.
Fungus actinomyces.

Many of these bacteria may reach, through certain channels which will be described later, various parts of the body where they will cause disease, but also the protein poisons formed in the focus by bacterial activity may become absorbed. These poisons or toxins are derived from the molecular disruption of the invading organisms setting free the intercellular toxins and by the bacterial metabolism; the by-products of the extra- and intracellular ferment action of both the pyogenic and saprophytic bacteria are almost always relatively strong poisons to the host. Various colored pigments are formed which have not been studied very much. From nitrogenized bodies or protein bodies, which constitute the greater proportion of animal tissue, there are formed complicated protein poisons, ammonia, ptomains, alkaloids, hydrogen sulphid, aromatics (indol, skatol, phenol, tyrosin), and gases such as nitrogen. From carbohydrates and animal fat there are formed acids (lactic acid, formic acid, acetic acid, butyric acid) and gases (carbon dioxid, nitrogen, methane, hydrogen). These by-products are usually easily recognized by the odor. Let him who doubts the danger of infected teeth and pus pockets be present at the dental operation and in close proximity to the foul, pus-soaked, discolored tooth, the ill-fitting crown or fixed bridge that is removed, and he will soon be convinced that such substances, if absorbed into the system, must be injurious to the health.

Frequency of Oral Infections.—Most of the infectious lesions of the mouth are of chronic character; quite frequently they are not noticed by the patient and have started and existed for a long period without local symptoms. As no special complaint is made by the patient, such diseases may develop under the very eyes of the dental practitioner, who, as a rule, spends little time in making a thorough examination of the mouth and adjacent parts, being too busy with his routine work and its many important and com-

plicated details. These chronic lesions are just the ones which are so frequently the cause of focal infections. To show the frequency of oral lesions Black[3] had roentgenograms of all the teeth of 300 patients taken. These examinations were not made because of any definite indication or dental complaint, and consequently represent as nearly average conditions as can be obtained. The following tabulation gives the results:

Age.	Number of patients.	Average number of teeth per person.	Percentage of persons having infections of the maxillary bones.
Under 25	86	30	56 per cent.
25–29	53	29	72 per cent.
30–39	68	26	87 per cent.
40–49	53	25	89 per cent.
50 and over	40	23	100 per cent.

To show the frequency of oral infections in patients at a hospital for chronic diseases let me cite the result of my first examination of the patients at the Robert Breck Brigham Hospital: I examined 81 patients; oral infections were present in 72 patients, or 90 per cent. Of the remaining 9, 2 had a mild pyorrhea, 6 needed fillings and restorations, and only 1 did not need any dental attention. I have extracted 334 teeth from the 72 patients on account of abscesses and severe pyorrhea.

Pathology of Oral Infections.—Acute alveolar abscesses are seldom neglected by the patient on account of the alarming symptoms which accompany the disease. The infection usually occurs at the end of a root and in such cases is transmitted from an infected dental pulp. The fibers of the peridental membrane, which have a wonderful resisting power, are infiltrated with pus which finally destroys the peridental tissues and spreads in the cancellous part of the bone. In this state we call it an acute alveolar abscess. The pus, having no outlet and being under pressure, involves the Haversian canals, which furnish a passage to the outside of the bone where the pus first collects under the periosteum. The periosteum is elevated from the bone and the patient experiences extreme pain. The temperature rises, the gum shows a swelling of red appearance, accompanied by a widely distributed edematous swelling of the face. This condi-

tion is called a subperiosteal abscess. When finally the periosteum is penetrated the symptoms become less marked; the pus collects under the gums and is called a subgingival abscess. The mucous membrane shows a light spot where the abscess points and where the pus will find an outlet to the mouth or face. The disease so far has been a process of destruction and if the condition is left to itself or after unsuccessful treatment the process of reparation begins. This attempt at healing consists in formation of granulation tissue, and the abscess is now called a chronic abscess.

Chronic Alveolar Abscess.—After the pus has found an outlet, the symptoms of the inflammation gradually disappear, the surrounding tissues having been rendered immune. Pus discharge from the sinus, however, continues just the same as long as the cause remains. The chronic inflammation may be kept up by the necrotic dental pulp which has only been partially removed or has not been removed at all, or it may be due to the condition of a root apex which forms an obnoxious foreign body if it becomes denuded from the peridental membrane; impregnated with pus or partly absorbed, as seen in Figs. 152–155. Therefore it frequently happens that the patient, who has no more discomfort believes the abscess entirely cured, while all the time it continues in a chronic stage, discharging pus from a sinus into the mouth, where it is mixed with saliva and disintegrates the food.

Acute Abscess Due to Difficult Eruption of Teeth.—Subperiosteal or subgingival abscesses are sometimes caused from difficult eruption, especially of the lower wisdom teeth, but malplaced cuspids and upper wisdom teeth may also give rise to an infection. In most cases the infection occurs after the gum has been pierced by the erupting cusps and may be due to food and fluids of the mouth entering through this wound. The soft tissue does not adhere to the enamel of the crown as it does to the cementum on the root by means of the peridental membrane and ligamentum circulare, and therefore foreign material is free to pass deep into the tissue around slowly erupting teeth, both impacted and normal. In other cases the infection is due more to irritation of the gum which is crowded over the occlusal surface during mastication and becomes bruised by the teeth of the

opposite jaw. In the back of the lower jaw where there is no natural drainage the pus accumulates and the inflammation often

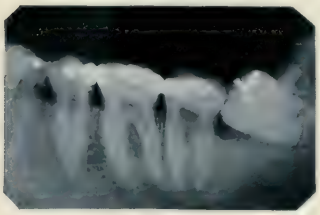


Fig. 152.

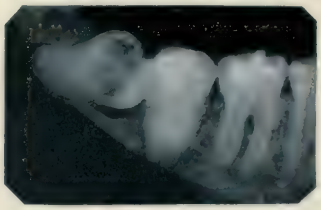


Fig. 153.

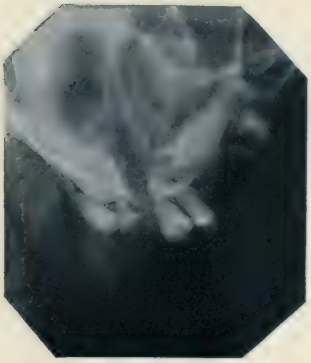


Fig. 154.

Fig. 155.

Fig. 152.—Roentgenogram showing partly erupted tooth which had become infected.

Fig. 153.—Roentgenogram showing an impacted lower third molar with a large cavity and a crown accompanied by infection, with a great deal of pus discharge around the tooth, swelling of the surrounding tissues, trismus of the muscles of the jaw, and difficulty in swallowing.

Fig. 154.—Roentgenogram showing two cuspids which have been partly eroded, due to an abscessed condition which was probably caused by an infection from the stumps of the remaining teeth. There was a great deal of pus discharge through a sinus on the palate.

Fig. 155.—Roentgenogram of an unerupted lower cuspid, showing erosion of the crown due to an abscess condition. There was a great deal of pain and swelling in the region of the lower lip. Pus was discharged through a sinus into the mouth.

involves the fauces, the mucous membrane, and the muscles about the ramus, a pharyngitis may set in, deglutition often becomes difficult, and trismus of the muscles of mastication is a common

occurrence and is sometimes so marked that the patient is unable to open his mouth. Fever, severe pain, and glandular enlargement are generally present, and I have seen cases where the abscess extended way down into the neck. Unerupted teeth may

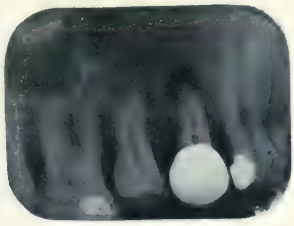


Fig. 156.

Fig. 157.

Fig. 156.—Roentgenogram of an upper bicuspid with a gold crown. The pulp apparently has become infected and caused the blind abscess indicated by the black area at the end of the root.

Fig. 157.—Dry skull showing a similar condition and demonstrating the cause of the black area shown; namely, destruction of bone around the end of the root.

also become infected from abscesses on neighboring teeth (Figs. 152–155).

Dental Granulomata or Blind Abscesses.—In the last decade teeth have been devitalized for several reasons without realizing the danger of such proceedings, and the result of imperfect root canal work was not known until roentgenology was developed for

dental use. When the so-called areas of lessened density were shown in roentgenograms at the apices of devitalized teeth little attention was paid to them. They were considered a negligible quantity because the patient had no alarming symptoms of disturbance and often not the slightest discomfort. It was considered good dentistry to retain such teeth rather than lose an important organ of mastication, but since the pathology and bacteriology of these symptomless lesions have been studied more carefully and since the important discovery of focal infection, we

Fig. 158.—Photomicrograph of a tooth root with blind abscess or dental granuloma.

have come to realize the great fact that such septic conditions about the teeth may be more dangerous than the violent, acute conditions, principally on account of their deceiving nature and because they undermine the patient's general health.

The dental granuloma or blind abscess is caused by reaction of the peridental tissues to mild injurious agents such as bacteria in small numbers and of low virulence, bacterial toxins, or small amounts of necrotic tissue. It is characteristic of the lesion to start and continue to grow for a long time without the patient's knowledge and without symptoms of inflammation. It can be

compared with a circumscribed osteomyelitis. Inflammatory chronic new formation of tissue occurs at the apex of the root and grows at the expense of the bone (Figs. 158 and 159).

While granulomata occasionally attain large proportions, they usually remain about the size of a pea. The seat of chronic inflammation is surrounded by a fibrous capsule which extends into the medullary spaces between the trabeculæ of the bone. This is the reason why in most cases the granuloma is held back in the

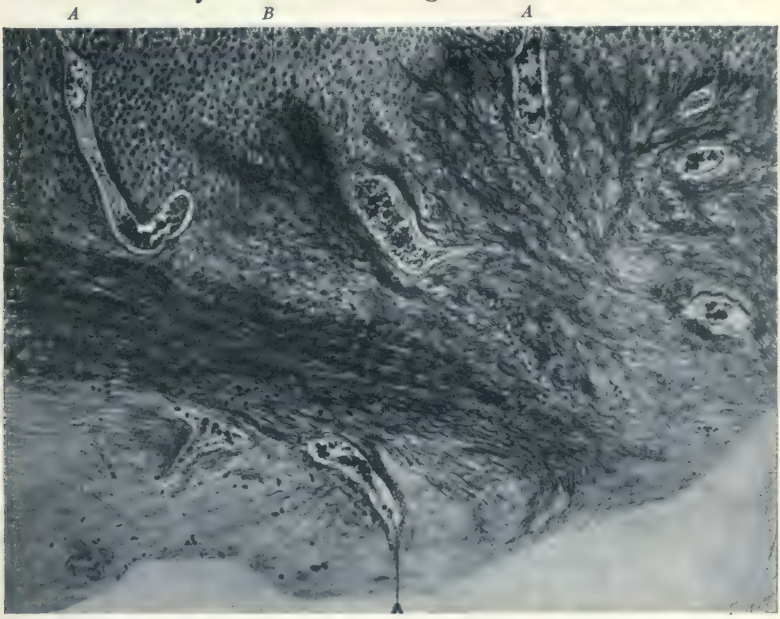


Fig. 159.—High-power drawing of the fibril capsule of the granuloma shown in Fig. 158, illustrating its fibrous make-up and penetration by many vessels: *A*, Vessels; *B*, inner part of granuloma.

jaw when the tooth is extracted. It is, however, occasionally connected so firmly with the peridental membrane that it stays attached to the extracted tooth. The thickness of the capsule varies greatly. The fibers are arranged in bundles and grow in various directions, as can be well demonstrated with special stains, such as Mallory's phosphotungstic acid—hematoxylin method (Fig. 159).

The study of the capsule impresses on us the great effort of

nature to wall off the seat of inflammation so as to prevent spreading into neighboring parts. It also demonstrates that this capsule does not prevent absorption, as it contains a meshwork of capillaries and is penetrated abundantly by larger vessels, thus establishing direct communication from the inner part, the seat of inflammation, with the circulation. Bacteria and toxins may, therefore, be carried away by the blood-stream (Fig. 159). The inner part of the lesion appears to be but one large mass of plasma

Fig. 160.—Photomicrograph showing a root end with a granuloma containing many dilated vessels crowded with red blood-corpuscles.

cells infiltrated in the inflammatory granulation tissue. Careful examination reveals capillaries which are often lined by only a single layer of endothelium and occasionally are extremely dilated and crowded with blood-corpuscles (Fig. 160). Polymorphonuclear and endothelial leukocytes and eosinophils may be found in large or small numbers according to the special condition which produced the tissue reaction. Quite frequently we find one or two places in the granuloma where necrosis has taken place, and a cer-

tain number of cells are seen detached from the rest and are more or less broken down. Polymorphonuclear leukocytes are then found in large numbers in the capillaries and in the tissue where the process of destruction is going on. The pus which is formed may be seen in the central part of the granuloma, which may contain also remnants of the decomposed tissue as well as

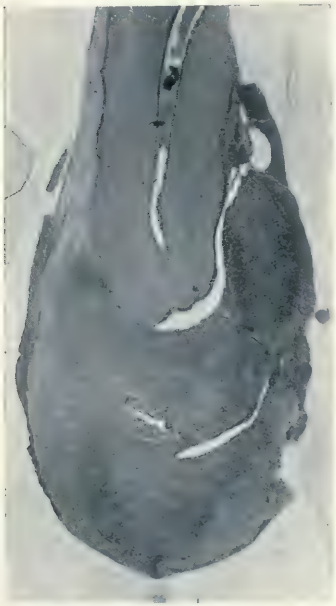


Fig. 161.—Photomicrograph showing large granuloma with pus formation in the center.

Fig. 162.—Photomicrograph showing root apex with a granuloma in which the suppurative process has broken through the capsule, forming a sinus.

inflammatory excretions from the pulp canals. The process of suppuration is seldom very severe and the pus is usually absorbed. Occasionally, however, the destructive process becomes more extensive, tearing down the fibrous encapsulation and forming a sinus to the surface of the gums or face (Fig. 162). The condition of the root end, which is always involved in this type of lesion, is of great importance. The cementum of the tooth, as a

rule, becomes denuded of the peridental membrane. It easily absorbs the products of inflammation and becomes infected, forming an obnoxious foreign body which nature tries to eliminate. Absorption starts at the surface and soon the cementum presents a rough appearance which is too minute to show in a roentgenogram. It is, however, easily recognizable under the microscope and due to osteoclastic absorption as seen in photomicrograph (Fig. 163). The absorption of the tooth root is very slow and

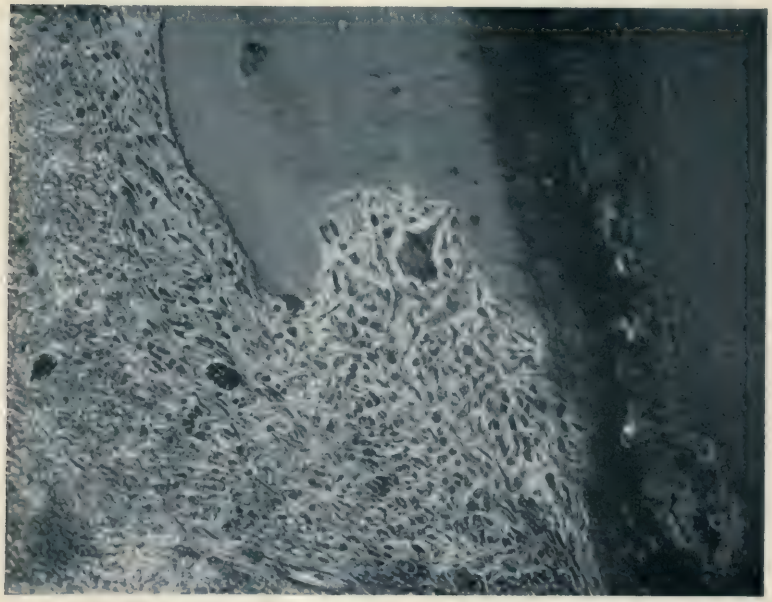


Fig. 163.—Photomicrograph with high power showing part of a root and granuloma. Note large osteoclast at the absorbed surface of the tooth.

differs somewhat from the same condition in the bone; there the dead part may finally become separated and expelled as a sequestrum, while in a tooth we find gradual absorption only of the root. It starts at the apex, and soon involves also the dentin (Fig. 164). This condition of the root apex is of the greatest importance when it comes to the treatment of such blind abscesses. There is to my knowledge no medicament, nor method, germicidal, oxidizing, or electrolytic, that will revivify a pus-

soaked, partly absorbed tooth apex, and as long as it exists it remains the cause of disease.

Periodontal or Radicular Cysts.—Remnants of epithelium of the embryonic enamel organs are commonly found in the normal peridental membrane, and therefore we may find them in the dental granuloma or blind abscess. The irritating influence of the chronic inflammation causes them to proliferate, and we

Fig. 164.—Photomicrograph of a root end with granuloma showing absorption of a large amount of cement and dentin.

Fig. 165.—Photomicrograph of an epitheliated granuloma showing band of epithelium proliferating through the granulation tissue.

therefore often find dividing and branching chains of epithelium which grow like a network through these lesions. In a section they show as bands of uneven thickness radiating in various directions. The cells of the proliferating epithelium become large, and the cytoplasm and nucleus grow more distinct. Leukocytes and plasma cells often invade the intercellular substance which loosely connects the various cells.

Cyst Formation.—If necrosis occurs in the center of an epi-

theliated granuloma, we find that the epithelial strands have a tendency to grow between live and necrosed tissue, sometimes giving the appearance of an endeavor to encapsulate the tissue which has become destroyed. Such epithelial linings may actually be found to cover the entire inner surface of the granuloma, which must be looked upon as the beginning of a periodontal or radicular cyst (Fig. 166). The exudates accumulating in the

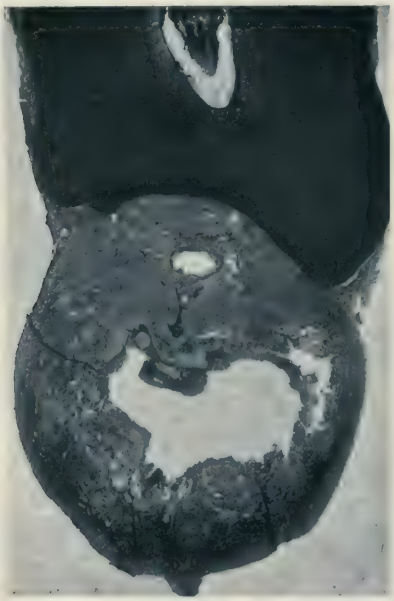


Fig. 166.—Photomicrograph of an epitheliated granuloma showing the beginning of a cyst. Epithelium is growing over part of the surface of the lumen. Note also rhomboid spaces due to cholesterin crystals.

lumen cause extension of the cyst, which may grow to the large size with which we are more familiar clinically. A careful study of the history and pathology of this type of bone cyst shows that they are of infectious nature. Roentgenographic examinations give further evidence of this by demonstrating that such cysts are almost always connected with a devitalized tooth except in cases where a tooth has been extracted without removing the epitheliated granuloma or the partly formed cysts (Fig. 167).

Pus Pockets and Pyorrhœa Alveolaris.—Pus pockets are quite frequently found on single teeth and are due to infection of the marginal part of the peridental membrane with involvement and destruction of the bone which forms the alveolar socket. They are caused by injury or irritation such as comes from poorly fitted gold crowns or fillings, from lack of contact between two

Fig. 167.—Roentgenogram of a jaw showing a large periodontal cyst. This was caused by a dead tooth which is seen extending into it and which has a root canal filling. The cyst contained pus.

teeth, causing food to crowd and stagnate in the interdental spaces, or from ligatures and rubber-dams left around the neck of a tooth.

Pyorrhœa alveolaris, or Rigg's disease, is a chronic condition of extremely frequent occurrence and usually involves all or nearly all of the teeth. It starts with inflammation of the gums, which may be due to local causes, such as lack of hygiene, aëration and

massage, and the irritating influence of salivary calculus or malocclusion, but frequently is brought about or associated with systemic disturbance, especially gastro-intestinal disorders, overfeeding, lack of exercise, gout, and diabetes. The inflamed and congested gums become relaxed and give access to the deeper tissues, namely, the peridental membrane and the alveolar bone

Fig. 168.

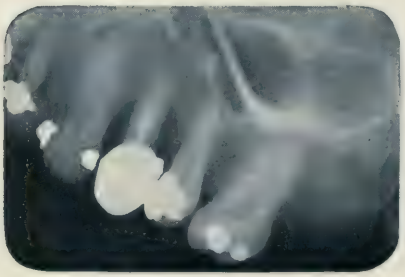


Fig. 169.

Fig. 168.—Photograph of a dry skull with pus pockets around the upper first bicuspid (the tooth in the center of the picture). This is probably due to lack of contact of this tooth with the neighboring one.

Fig. 169.—Roentgenogram of a similar condition caused by an ill-fitting gold crown. Note the extent of the pus pockets on both sides of the tooth.

which furnishes support to the teeth (Fig. 168). Infection soon sets in, the process being a chronic suppurative inflammation during which more or less serumal calculus is deposited at the sides of the teeth, which in turn increases the chronicity of the disease. The process of destruction proceeds, as a rule, in a longitudinal direction of the tooth, and therefore we find quite

frequently a very deep pus pocket at one side of the tooth, while at another the bone is normal. As the bone disappears,

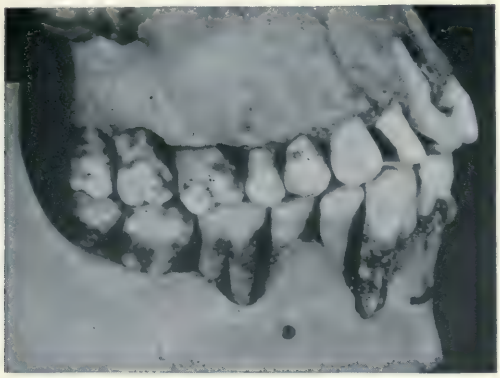


Fig. 170.

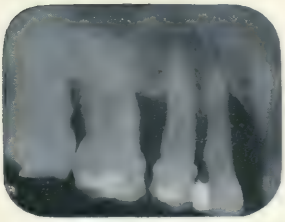


Fig. 171.

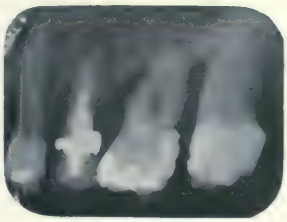


Fig. 172.

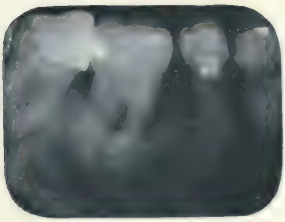


Fig. 173.

Fig. 174.

Fig. 170.—Photograph of a dry skull showing pyorrheal affection. Note the destruction of the alveolar process on various teeth.

Figs. 171–174.—Roentgenograms of a mouth affected by pyorrhea. Note the absorption of bone around the teeth and deep pockets at various places. One bicuspid in Fig. 172 shows, in addition, a blind abscess or dental granuloma.

the tooth becomes looser and looser and so loses its functional efficiency (Figs. 170–180). The pus which is constantly formed

discharges into the mouth except in cases where the opening of the pocket becomes closed up. In such cases we quite frequently get the formation of an abscess which may take on an acute course, the pus collecting under the periosteum or under the gum. Bacterial infection is more or less accidental. There are always

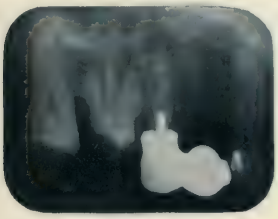


Fig. 175.

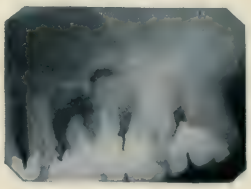


Fig. 176.

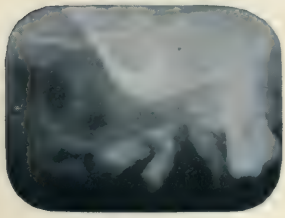


Fig. 177.

Fig. 178.

Fig. 179.

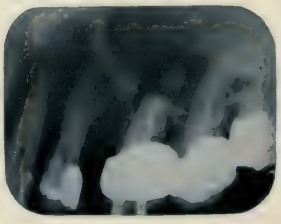


Fig. 180.

Figs. 175–180.—Roentgenograms of various patients who suffered from maxillary sinusitis. Each picture is of a separate case, showing the condition of the upper teeth on the side of the infected antrum.

streptococci, staphylococci, and various bacilli, as well as many saprophytes present, of which the Treponema mucosum plays an important rôle. Noguchi discovered that this spirillum gives the peculiar odor to the pyorrhea pus. The Endamœba buccalis which has been found by Barrett and Bass is also often found in unclean mouths, but is of no etiologic importance.

The Mode of Distribution of the Infection in Oral Focal Disease.—1. *Disease Transmitted by Continuity.*—The surrounding structures of the oral cavity may become infected from infections of and about the teeth. Necrosis of the palatal bones, abscesses in the floor of the mouth and in the pharynx are liable to occur, while infection of the nose and especially the maxillary sinuses is a very common trouble.

2. *Infection of the Gastro-intestinal Tract.*—Dental abscesses with sinuses and pus pockets discharging into the mouth where the pus mingles with the saliva and food during mastication cause infections of the throat and reach the stomach and intestines, giving rise to most serious diseases of the mucosa of the alimentary canal. For a long time the acids of the stomach have been looked upon as destructive to such bacteria, but Smithies,* in a microscopic examination of gastric extracts from 2406 different individuals with "stomach complaint," showed that, irrespective of the acidity of such gastric extracts, bacteria were present in 87 per cent. Hunter says there is a limit to the power of the stomach to destroy such organisms. Even in health it is never complete and is solely due to the presence of free HCl. But these powers become progressively weakened when, through any cause, an increased and continuous supply of pus organisms is associated with a diminished and continually lessening acidity of the gastric juice.

3. *Lymphogenous Infection.*—Lesions of the oral cavity are quite often associated with secondary infections of the lymphatic vessels and lymph-glands of these parts. There are two groups of lymph-glands which drain the jaws and teeth and their mucous membrane. The submental glands take care of the region of the lower incisor teeth. Still more important because of the greater frequency of their involvement are the submaxillary lymph-glands. They are three in number and drain the rest of the teeth and their investing tissue. All of them are tributaries of the lymph-nodes of the neck. The submaxillary lymph-glands, which are hardly noticeable when in normal condition, become quite frequently involved. The reaction varies in character ac-

* Cited from Mayo: Mouth Infection as a Source of Systemic Disease.

cording to the virulency and character of the invading bacteria. Lymphatic infection occurs most often in children, but is not at all rare in adults. The entrance of the tubercle bacillus by way of the teeth is, perhaps, more common than we think, Professor Cantani, of Naples,[4] has reported 50 clinical cases of tubercular infection of these lymph-glands through the teeth.

Hematogenous Infection.—Today we know that infections are never entirely localized. Bacteria, their toxins, and bacterial poison produced during the process of infection and inflammation, or both, are always absorbed into the circulation, not only from the primary focus but also from secondary lesions. The presence of bacteria and of protein poisons in the blood may cause diseases of violent and acute symptoms, but more frequently cause secondary disturbances of latent and chronic character and many lesser ills, such as malaise, fatigue, and other subjective symptoms, soreness of joints, muscles, and nerves. Lesions without any direct outlet, such as blind abscesses and periodontal cysts, are very liable to be the source of hematogenous absorption.

4. *Oral Infection as an Indirect Factor.*—The fact that a coexisting infection in the mouth may be a considerable burden on a body weakened by some other disease has already been discussed and clearly illustrated in the charts in Figs. 150 and 151. The continuous fighting of the infection and elimination of the poisons produced must be a great tax on the organs whose function it is to combat disease. Therefore, for this reason alone we should search for and eliminate diseased conditions in the mouth in order to raise the resistence and improve the patient's general health.

6. *The Teeth as a Source of Subjective Symptoms of Pressure and Nervous Disorders.*—The extensive area of distribution of the trifacial nerve and its frequent communications with other cranial nerves and the sympathetic system explains the clinical observations that pain and irritation originating from some dental or oral cause may be referred to very distant parts of the face and head, including the ear (otalgia dentalis), the eye, the nose, and accessory sinuses. Such pain may be continuous, intermittent, or periodic; it may be intense, sharp, throbbing,

or dull, and it may be a sensation of obscure, indefinable pressure. It sometimes results in more serious nervous disorders, such as insomnia, melancholy, and epilepsy. The suffering that goes with these affections is usually intense, especially if it has lasted any length of time and the cause is often difficult to ascertain and involves a most careful study with temperature and electric tests, as well as extensive and painstaking roentgenographic examination. The most important causes are impacted and unerupted teeth, obscure pericemental inflammation and affections of the dental pulp, such as irritation from improper filling, pulp nodules or stones, infection from obscure decay, either starting underneath the gum or continuing after a tooth has been filled, due to insufficient sterilization.

SPECIAL AND GENERAL DISEASES WHICH MAY ORIGINATE FROM SOME ORAL CONDITION

In the following list I have tried to enumerate some of the special and general diseases which may have their origin in the oral cavity. It may not be amiss, however, to state here that I do not mean to imply that diseases of the teeth are the only or even the most important etiologic factor in all these disturbances. Neither have I presumed in compiling this list to collect all the claims that have been made for focal infection in general and dental lesions in particular, but have aimed to be conservative.

Laryngology, Rhinology, and Otology.—*Maxillary sinusitis* in its various forms is much more frequently due to a dental infection than has heretofore been supposed (75 per cent. according to Brophy). Its chronic form develops quite frequently without the patient's knowledge and often is only discovered by accident. The upper molars and bicuspids should be roentgenographed in all cases of maxillary sinusitis, and the dentist should in turn advise his patient to have his sinuses investigated should he find suspicious upper back teeth.

Nasopharyngeal adenoids are often caused by mouth-breathing and malocclusion of the teeth, and particularly by narrow and compressed arches.

Tonsillitis and *pharyngitis* may be caused by oral sepsis.

Otalgia Dentalis.—Referred pain may be due to a cause in the upper or lower jaws.

Otitis media sometimes has a referred nerve irritation from a dental condition as a predisposing cause.

Ophthalmology.—Ophthalmic disturbances due to oral conditions may be brought about in either of two ways, through nerve irritation or through hematogenous infection.

Infectious conjunctivitis in children may be caused by carrying the infection with the fingers from an infected aching tooth to the eye.

Acute iritis can be caused by nerve irritation or hematogenous infection from the nose or mouth.

Chronic iridocyclitis and *choroiditis* are usually combined with iritis.

Keratitis also comes from direct and indirect infection.

Retrobulbar neuritis occurs from hematogenous infection or from infection of ethmoids or sphenoids.

Orthopedics.—*Infectious arthritis, acute* and *chronic,* are now accepted as being due to focal infection. The nasopharynx, the oral cavity, and the gastro-intestinal tract are supposed to be the most important sites of the focus. Cases of acute multiple arthritis from a dental cause are not uncommon. Cause and effect can be ascertained more easily in this type of arthritis, especially as the removal of the focus is almost always promptly followed by disappearance of the disease, which may be preceded, however, by an exacerbation. In the subacute and chronic types of the trouble the result, as a rule, is not so gratifying. The joints themselves are often a secondary focus, from which the infection may be further transported, while quite frequently they show tissue changes which are beyond repair from an anatomic point of view. The removal of the focus, however, usually relieves symptoms of pain and swelling from subacute conditions and prevents reinfection from this source.

At the Robert Breck Brigham Hospital for chronic disease the treatment of chronic arthritis is directed toward improvement of the functional efficiency of the patient. To achieve this the patient's general health is first built up not only by dietary

measures, but by the removal of any infectious lesions and the correction of all abnormal conditions which may lower the patient's resistance and prevent improvement of his condition.

Pediatrics.—*Acute rheumatic infection* in children, including *endocarditis* and *nephritis*, may be caused by foci in the nose and throat or by dental infection.

Arthritis may come from foci in the same location.

Lymphadenitis in the glands of the submaxillary region and neck often occurs from infections about the teeth, including the entrance of the tubercle bacillus through this channel.

Nervous and abnormal *mental conditions* are often found which are due to pressure from impacted teeth.

General Medicine.—*Septicemia*, *pyemia*, and *toxemia* may be caused by diseases of the teeth and jaws, but are of comparatively rare occurrence, while a great many vague medical conditions, due to absorption of a slight amount of toxin or bacteria, are exceedingly common. A perfectly healthy person may be able to eliminate this daily dose, but, as a rule, sooner or later a condition arises which brings about more serious results. Lowering of the body temperature by exposure to cold or wet may bring about more or less vague rheumatic conditions of the muscles, joints, and nerves. Other expressions of chronic toxemia are frequently occasioned by diseases of the teeth and jaws, that is, disproportionate fatigue from slight exertions, inability to do the accustomed day's work mentally or physically, benumbed mental activity, requirement of an abnormal amount of rest, loss of weight, grayish, sallow skin, and a rise in the temperature in the afternoon or evening. Leukocytosis and secondary anemia are also often observed.

Endocarditis and *nephritis* caused by focal infection may have their etiologic factor in the mouth. In heart infections we must consider, in addition, the danger and additional strain on the heart caused by toxic absorption and its elimination, as has been demonstrated in some of the charts.

Gastro-intestinal disorders caused by pus from the nasopharynx or mouth include, according to many writers, septic gastritis, appendicitis, colitis, and gastric and duodenal ulcers.

Ductless Glands.—Toxemia from oral sepsis may affect the glands of internal secretion, and it is conceded that overstimulation by the toxins may produce symptoms of hyperthyroidism. High blood-pressure and the resulting circulatory disturbances are caused by the same toxic condition, affecting directly or indirectly through the glands of internal secretion the vegetative nervous system controlling the vasomotor system.

Neurology and Psychiatry.—*Affections of the trigeminal nerve* and referred pain to the nerves with which it communicates may be due either to dental lesions or conditions exerting pressure.

Melancholy, mental depression, insomnia, and similar symptoms of more or less obscure nature may likewise be associated with some hidden dental condition, as has already been described in another place.

THE IMPORTANCE OF INVESTIGATING THE MOUTH

All this demonstrates the importance of dental research work, which will develop dental science along therapeutic lines, while heretofore it was principally concerned with perfecting mechanical skill. Also it will bring about its proper relation to medicine, to which it is naturally allied, and of which it should form a department like other specialties.

It further brings out the importance of the service which properly trained dentists can render the internist by intelligently examining the mouth of a patient, with the knowledge in mind of its relation to somatic diseases.

The relation of dentistry to other specialties is of the same importance. The dentist should consider the condition of other parts, especially adjoining ones, the nose, throat, and sinuses, while in diseases treated by other specialists the etiologic or complicating factor may be found in the mouth.

A short description of the pathology of some of the more common dental diseases was added to show that they are a special study in themselves of numerous different clinical aspects arising from a variety of causes, and that their correct diagnosis requires special training. The statements encountered in the literature which sets forth the fact that in a certain disease the teeth were in

so many cases good, in so many fairly good, and in the rest bad gives us as little information as would statistics showing that a certain number of patients were in poor health and another number were in fairly good condition.

I have also intended to show that foci in the mouth, as well as in the adjoining parts, the nose and throat, may be manifested only by remote general symptoms, and that if such symptoms indicate focal disease, pathologic conditions of the teeth and jaws should be suspected, and, like other parts, the mouth should be carefully investigated.

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PATHOLOGIC HEMORRHAGE

A Group of Cases Illustrating This Condition with a Note on the Early Diagnosis of Pernicious Anemia.

The Methods of Demonstrating the Abnormalities Associated with the Coagulation of the Blood; The Importance of the Blood Platelets; Chronic Congenital Purpura Hemorrhagica; Its Distinction from Hemophilia; Idiopathic Acute Purpura Hemorrhagica and Its Distinction from Aplastic Anemia; Purpura Rheumatica and Its Diagnosis from Purpura Hemorrhagica; Early Tongue Symptoms of Pernicious Anemia; Secondary or Symptomatic Purpura Hemorrhagica; Bibliography.

I WISH to show you a group of hemorrhagic cases and to discuss somewhat the methods of demonstrating the abnormalities associated with the coagulation of the blood. I wish to lay particular stress on those cases with diminished blood platelets—cases of purpura hemorrhagica—and on the importance of these small formed elements of the blood.

In the study of the blood the only formed elements which receive attention, as a rule, are the red cells and the white cells. The third formed element of the blood, the blood platelet, has received relatively little attention. This element has very positive and important features, and there are certain conditions attributable to its pathologic alteration. The platelets have been recognized as separate entities of the blood since Bizzozero and Hayem in the '80's first worked with them. They are, as shown by Wright, fragmented particles of protoplasm derived from the giant cells (megakaryocytes) of the blood-forming

organs. They undergo a peculiar viscous metamorphosis when the blood clots.

Hemorrhagic conditions due to a recognized abnormality of the blood are associated with a diminished number of platelets, or with alterations of these elements, or of other factors involved in the coagulation of the blood, and are in some instances perhaps dependent upon a fibrinolytic ferment. The various types of purpura hemorrhagica, hemophilia, melena neonatorum, the hemorrhages occurring in certain liver conditions belong to this group. Such cases may have spontaneous hemorrhages from one or more mucous membranes of the body, or an undue amount of hemorrhage following injury, or hemorrhages into the skin, muscles, joints, or other tissues. There are certain cases that have hemorrhages into the skin, but do not have hemorrhages from the mucous membranes or an undue amount of hemorrhage following an injury, which show no recognized abnormality of the blood, for example, purpura rheumatica and purpuras caused by drugs. There are cases of endocarditis that develop purpuric-like areas, particularly on the hands, that are due to bacterial embolism and are not attributable to alteration of the blood-coagulation factors. Scurvy is essentially the only condition where there may perhaps occur spontaneous mucous membrane hemorrhages with no clear-cut recognized abnormality of blood coagulation. Hemorrhage from chiefly or entirely one source is not infrequently considered as due to some blood abnormality, but with a careful study of the case it is usually found that the hemorrhage is due to local conditions and is not dependent upon any general condition of the blood.

A careful study of the blood should be undertaken in all hemorrhagic conditions. This careful study should particularly include, properly performed, the following tests: enumeration or estimation of the platelets, coagulation time, bleeding time, firmness, and retractability of the clot. In many cases with pathologic hemorrhage these tests will yield positive information. Before I take up the cases I will discuss somewhat these tests.

1. *Enumeration or Estimation of the Blood Platelets.*—Normally the blood platelets in man vary between 200,000 and

400,000 per cubic millimeter, averaging about 250,000. When they are below about 60,000 spontaneous bleeding usually occurs, and when below 20,000 bleeding always occurs. The platelets may be counted by Wright and Kinnicutt's method or by Pratt's, in a manner similar to that used in counting the red and white corpuscles. The technic is, however, more bothersome and it requires considerable experience to make a reliable count of these elements. One with some experience may in a shorter time and more easily derive sufficient information for the purposes of diagnosis from a simple estimation of the number of platelets from blood-smears instead of by an actual count. By so doing one can tell whether they are greatly or somewhat increased, about normal, somewhat, markedly, or greatly diminished. Neatly and quickly made blood-smears properly stained with one of the modifications of Romanowsky's stain, preferably Wright's modification, will serve to estimate the platelets as one may similarly estimate the white count. However, we much prefer to estimate the platelets from a smear of fresh blood stained with brilliant cresyl blue because the platelets are more readily seen as separate objects than in the fixed preparation, and with this stain their granules and structure become evident. It is exceedingly simple to stain blood with cresyl blue, and may be done as follows: A fresh watery solution of 1 : 300 of this dye is allowed to dry on a glass microscope slide; once the stain has dried, it keeps indefinitely. A drop of blood is obtained on a cover-glass and quickly inverted on to the dried cresyl blue on the slide, so that the blood spreads out between the cover-glass and slide. The blood dissolves the stain and the platelets are stained blue. This method of staining is also very valuable for demonstrating the reticulated red cells or skeined cells, which are young red cells and normally form about 0.7 per cent of the red cells. These cells are not demonstrable as such in ordinary fixed and stained smears.

2. *The Bleeding Time.*—This is determined by simply pricking the ear with a clean, sharp needle and wiping upon blotting-paper every one or two minutes the drops that form, noting the time it takes for such a hemorrhage to cease. Normally such a

hemorrhage ceases in less than three minutes, and the drops rapidly diminish in size. In extremely abnormal cases such a hemorrhage may last for even hours unless suitable means are taken to check it. It is to be noted that the bleeding time, this tendency to bleed from fresh cuts, is independent of the coagulation time. One of the factors on which the bleeding time depends is the platelets. Roughly, the fewer the platelets below 125,000, the longer the bleeding time. There are, however, other factors which influence the bleeding time, as diminished amounts of fibrinogen.

3. *The Coagulation Time.*—This should be determined by some method that causes as little admixture of tissue juice as possible, because this substance which has a similar action to the blood platelets is very potent in accelerating coagulation. Thus, it is highly desirable to determine the coagulation time from blood derived from a vein, as of the arm, rather than through the tissues, as from the ear. A very suitable method for determining the coagulation time is that originally described by Morawitz and Bierch, and modified by Howell, Dochez, and Lee and White. Lee and White's method consists in determining the time it takes 1 c.c. of venous blood to just clot firmly in a clean glass tube that is 8 mm. in diameter so that the tube can be inverted without spilling the blood. By this method normal blood clots in from five to ten minutes. Variations in the amount of blood or size of the tube will, of course, cause variations in the coagulation time; also admixture of air, undue trauma, etc., hasten the coagulation time. Besides determining the time it takes the blood to clot firmly and throughout the sample, it is desirable to observe the time it takes for the first signs of coagulation to appear—that is, when the first fibrin strands begin to form or when the blood first begins to become thicker. This is because in some conditions the blood begins to clot in normal time, but does not completely clot for a longer time than normal. This is probably due to a slow rate of formation of thrombin or a diminished thrombin or fibrinogen content. Such a phenomenon is probably related to the reclotting phenomenon. This consists of noting whether the fluid surrounding a firm clot will

itself clot after the clot has been removed from the tube. Usually some minutes before complete coagulation one will observe that the upper surface of the blood has begun to clot. This superficial coagulation may be great enough to prevent the fluid blood beneath from running down the tube when it is tilted, and in such instances it is not uncommon to see a bubble of air travel through the fluid blood. One must thus be careful not to mistake such surface coagulation for complete coagulation. There are other methods perhaps preferable for determining the first signs of coagulation, but the one given serves very well for ordinary clinical purposes.

It may be noted here that the length of the coagulation time does not run parallel with the tendency to hemorrhages, for there are certain cases of hemophilia that bleed severely when the coagulation time is about twenty minutes, and others that do not do so when the coagulation time is one hour.

4. *The Firmness and Retractability of the Clot.*—Two other observations should be made on the clot—its firmness and retractability. A weak clot is associated with diminished amount of fibrinogen or thrombin. Normally the clot continues to retract from the sides of the glass tube for a period of hours and expresses serum. When the platelets are greatly diminished in number the clot never retracts at all. The degree of retraction is roughly proportional to the number of platelets.

The tests that I have mentioned are the most important ones for establishing the diagnosis of hemorrhagic conditions.

Besides these tests the following ones are valuable under certain conditions, but we will have no special reference to them in discussing the cases that I will presently show you. These tests are: 1. The effect of suitable amounts of calcium on the coagulation time and prothrombin time. 2. Determination of the prothrombin time, which is to determine the time it takes a sample of oxalated plasma to clot with the optimum amount of calcium. 3. Determination of antithrombin. 4. Determination of fibrinogen. 5. Determination of the presence of a fibrinolytic ferment.

Besides these laboratory tests on the blood, a clinical test

probably of some value in hemorrhagic diseases is to determine the effect of placing a tourniquet around the arm for some minutes and observing whether it causes any hemorrhages, large or small, superficial or deep, below the point of constriction. I will not discuss this test, but it may be noted that in hemophilia such pressure does not cause superficial hemorrhagic spots, while in purpura hemorrhagica it usually does so.

Let us now briefly consider the character of purpura hemorrhagica in the light of these laboratory tests and in its clinical features, and then I will show you cases of some of the types of this condition and discuss particularly how they differ from hemophilia, aplastic anemia, and purpura rheumatica.

Purpura hemorrhagica is a condition in which there is bleeding from one or more mucous membranes and usually purpuric skin lesions. In purpura hemorrhagica there occurs a marked diminution of the blood platelets, a prolonged bleeding time, and a normal or slightly delayed, rarely much delayed, coagulation time, and a non-retractile blood-clot that is usually soft. Purpura hemorrhagica is not to be confused with the other types of purpura, which have essentially a normal number of platelets and no definite alteration of their coagulation factors. Purpura hemorrhagica may be an idiopathic disease or appear as a symptom secondary to some recognized disease as pernicious anemia, lymphatic leukemia, diphtheria, tuberculosis, etc.

The idiopathic type may occur in the following forms: 1. Continuous, acute or chronic, acquired or congenital. 2. Intermittent. In the former the platelets are continuously below normal, while in the latter they are below normal during the attacks only. It is quite probable that the very chronic types, which are apparently often congenital, are of a different etiologic nature than that of the more acute types, though we have no real knowledge of the etiology of these conditions.

The case which I now present is an example of chronic, essentially continuous, congenital purpura hemorrhagica, which is so often confused with hemophilia. The condition is rare, but apparently not extremely so. During the past year we have observed 4 new cases at the Massachusetts General Hospital.

CASE 1.—The patient is a farmer twenty-two years of age who gives the following summarized history: His grandparents lived to be over sixty years of age, and his mother, father, brothers, and sisters are living and well. There is no family history of hemorrhagic disease. Except for measles, which was severe, he has had no infectious diseases. Off and on ever since he was born he has had nosebleeds and has had considerable difficulty in stopping them. Occasionally he has had slight bleeding from his gums. During his life he has always bled very profusely from small cuts. He got along very well until two years ago, when the nosebleeds became more frequent, occurring two or three times a week instead of only every few weeks, lasting often for three hours. Three weeks ago he had a severe nosebleed which lasted for three days; since then his nose has bled slightly every few days, but not within the past five days. During the past two weeks he has suffered from headache, ringing in the ears, palpitation, faintness, and slight dyspnea, and during this time he has grown paler. Never before has he felt sick or has he had to give up work or school. There has been no bleeding from other mucous membranes than those of the nose and mouth.

The physical examination shows a big framed man, appearing somewhat pale. The skin shows a long hemorrhagic scratch area over the upper chest, some very small petechiæ on the lower legs, and two superficial purpuric areas the size of a pea over the left abdomen, and two similar areas on the skin of the left side of the neck. On the upper arm is a deep ecchymotic area about 3 by 5 cm. which developed following slight trauma. The gums showed several minute hemorrhagic spots. The teeth are intact. Except for the above and a functional heart murmur the physical examination is entirely negative. The urine, stool, and Wassermann reaction are negative.

The blood examination shows the following: Blood platelets, 55,000; bleeding time, seven to ten minutes. The complete coagulation time, thirteen minutes; the initial coagulation began in six minutes; the clot does not retract. Hemoglobin 55 per cent. Red count 3,400,000. White count 9000; the differential

count shows polymorphonuclear neutrophils 54 per cent., lymphocytes 38 per cent., mononuclears 7 per cent., mast cells 1 per cent. The red cells in general are small and achromic; they show some variation in size and a little variation in shape, Polychromatophilia occasionally occurs. The reticulated red cells are 7 per cent.

The application of a tourniquet to the arm for five minutes produces numerous fine petechiæ on the arm considerably below the point of pressure.

The symptoms that he has had in the past two weeks are entirely attributable to the secondary anemia which has resulted from his hemorrhages. It is interesting to note that he says that he had measles severely, for when these cases have one of the exanthemata they usually do have them severely because the eruption is apt to become hemorrhagic due to their constant low platelet count.

This case could be diagnosed from the history and from the evidence given by the examination of the patient's skin at the present time even if no laboratory blood examination had been made. This is because there are but two hemorrhagic diseases that exist from birth—chronic congenital purpura hemorrhagica and hemophilia, and in hemophilia one never sees small superficial skin petechiæ. The blood examination, however, should always be made for its confirmatory evidence in such a case as this one, but in many others it is necessary for the diagnosis. (Another rare hemorrhagic condition especially causing nosebleeds is familial telangiectasis, but here we find a local cause for the hemorrhages.) Hemophilia was the diagnosis this patient was sent to the hospital with, but his condition is definitely to be distinguished from hemophilia. In hemophilia the blood-platelets occur in normal or slightly increased numbers, though they are physiologically or qualitatively defective, as pointed out by Fonio and Dr. Lee and myself, while in purpura hemorrhagica they are much decreased. In hemophilia the coagulation time and particularly the prothrombin time are nearly always much prolonged, while in purpura hemorrhagica these times are often normal and rarely much delayed, and never more than

slightly delayed in the congenital type. The blood-clot in hemophilia is firm and retracts in normal fashion, while it does not retract and is soft in purpura hemorrhagica. The bleeding time in hemophilia is usually essentially normal, while it is prolonged, not infrequently much prolonged, in purpura hemorrhagica. Superficial purpuric skin lesions do not occur in hemophilia, but do in purpura hemorrhagica. These lesions in purpura hemorrhagica may be very scant and minute and require careful inspection to discover them, and, too, they may be absent at any one given time. Big areas of ecchymosis, usually rather deep, do occur in hemophilia, and similar areas may occur in purpura hemorrhagica; in fact, most of our cases of congenital purpura hemorrhagica have shown especially on the extremities one to five hemorrhagic ecchymoses, usually rather superficial, with often a lump in the center probably due to the blood-clot. It would seem as if the cases of chronic purpura hemorrhagica apparently never had as extensive skin lesions as may occur in the more acute forms. The tourniquet does not cause petechiæ to appear in hemophilia, while it does usually cause them to appear in purpura hemorrhagica. Joint symptoms are common in hemophilia due to hemorrhage into the joints, and are rare in purpura hemorrhagica. Another most important point in the differential diagnosis of purpura hemorrhagica from true hemophilia is that hemophilia is hereditary through females and occurs in males only, while purpura hemorrhagica occurs in females as well as in males. There are certain cases of hemophilia where no family history of the disease is obtained; perhaps this is because the patient has no knowledge about his grandparents. In our series of cases there have been more females than males that have had this congenital type of purpura hemorrhagica. In women the presenting symptom may be excessive menstruation. Certain cases described in the literature as vicarious menstruation have undoubtedly been cases of chronic purpura hemorrhagica.

In regard to the prognosis of this type of case as compared to hemophilia I am at present unable to tell you, as such cases as these have not been followed long enough. There is perhaps some information to suggest that these cases become severer as

the patient grows older, while hemophiliacs appear to suffer less as they grow older.

The second case that I wish to show you is one of acute idiopathic acquired purpura hemorrhagica.

CASE 2.—The patient is a girl of eighteen. The history is negative except for the following: Six weeks ago she began to bleed from the nose and has continued to do so off and on since. During the past two weeks she has had continual vaginal flow and for the past week has noticed spots on her body. She has grown steadily paler and weaker. The physical examination reveals nothing of interest beyond the following: The patient looks pale and sick and has a temperature of 101° F. and a pulse of 100. There are scattered all over the skin, particularly on the lower legs, some fresh and some old, superficial, not raised purpuric areas varying in size from 1 mm. to 2½ cm. A few petechiæ appear on the mucous membranes of the mouth, and blood is oozing from the nose. The blood: The platelets as estimated from cresyl blue smears are exceedingly rare, about 5000 to 10,000. The bleeding time is forty-five minutes. The coagulation time and prothrombin time are slightly prolonged. The clot is soft and non-retractile. The red count is 1,300,000 and the hemoglobin about 25 per cent. The red cells show some achromia, considerable variation in size and shape, though no very large abnormal shaped cells occur, occasionally a normoblast is seen, and there is some polychromatophilia and stippling. The reticulated red cells are 10 per cent. The white count is 10,000; the polymorphonuclears 68 per cent.; lymphocytes 22 per cent.; mononuclear cells 10 per cent. Blood-cultures, Wassermann reaction, stools, urine, and other laboratory tests showed nothing of interest except for a small amount of fresh blood in the urine.

The diagnosis of purpura hemorrhagica is established by the marked diminution of the platelets. The case is of the idiopathic type because we find nothing for the condition to be secondary to. Such severe cases as this nearly always run an acutely fatal course and die some weeks to months after the onset of the disease. Those cases living for months have fluctuations in the intensity of the bleeding parallel with the rises

and falls in the number of the platelets, though these elements never reach normal. Some cases may have several attacks of purpura some months or years apart, with diminution of the platelets only during the attack, the earlier attacks usually being milder than the later ones. Such cases are known as the intermittent form of purpura hemorrhagica. Other cases may have mild attacks without recurrence. (This case continued to get steadily worse, bled from all mucous membranes, and died eight weeks after the onset of the disease. She refused to be transfused and no autopsy was permitted.)

It is to be noted that this patient shows a severe secondary anemia due to the hemorrhages. The blood-picture is that of secondary anemia following direct hemorrhage in a normal individual except for one important point, and that is that the platelets are not increased. So far as the red cells are concerned they have the characters of those of such an anemia and show evidence of regeneration, as evidenced by the increase of reticulated red cells and the presence of blasts and polychromatophilia. The polymorphonuclears are increased as occurs in the anemia following hemorrhage. In other words, we have evidence of activity of the red and white cell elements of the bone-marrow, but not of the giant cells of the marrow, the parent cells of the platelets. It is, however, quite possible that the platelets are formed readily enough, but that the difficulty is that they are rapidly destroyed in the circulation. There is some evidence that this may be the case because the marrow in cases like this may show plenty of giant cells and appear, as a whole, hyperplastic.

This observation on the activity of the marrow, as evidenced by the red and white cells, is important in distinguishing this and other acute cases of purpura hemorrhagica from idiopathic aplastic anemia, which has undoubtedly often been confused with it. Idiopathic aplastic anemia is a disease which runs an acute, progressively downward, fatal course of about three to six weeks' duration and characterized by absence of blood regeneration of any of the three formed elements originating in the marrow—the red cells, polymorphonuclears, and platelets. The marrow of such cases at autopsy is not hyperplastic, but typically shows

complete fatty degeneration. The red cells show no or very little evidence of regeneration, as evidenced by their slight variation in size and shape, the absence or rarity of polychromatophilia, blasts, and reticulated red cells. The white count is much diminished with a relative lymphocytosis, thus showing little or no regeneration of the white cells originating in the marrow. The absence in the peripheral blood of evidence of regeneration of the red and white cell elements is in contrast to the finding in cases of purpura hemorrhagica of regeneration of these elements. In common with purpura hemorrhagica the platelets are reduced because in aplastic anemia the megakaryocytes, the parent cells of the platelets, are destroyed along with the destruction of other cells of the marrow. It is to be noted that usually in aplastic anemia the anemia is evident early; gradually the platelets become fewer until reduced to so small a number that bleeding occurs; that is, it occurs relatively late in the disease, while typically in acute idiopathic purpura hemorrhagica bleeding occurs early. When purpura hemorrhagica has developed in a case of aplastic anemia we then rather arbitrarily call it secondary purpura hemorrhagica. It may well be that these two conditions, aplastic anemia and idiopathic purpura hemorrhagica, are not so distantly related, as is perhaps shown by the fact that cases may be recognized that appear to form an intermediate type of condition between them and suggest a partially depressed activity of the marrow especially involving the platelet elements. I have recently discussed this question in the Archives of Internal Medicine, 1917, xix, 1062.

In purpura hemorrhagica, primary or secondary, we may note that diminution of the platelets may be due to: 1. Destruction, depressed activity or exhaustion of the megakaryocytes (with or without similar action on the other elements of the marrow) by some unrecognized or recognized toxin or poison, as benzol, or by congenital absence of these elements. 2. Destruction of the platelets in the circulation. 3. Displacement of the megakaryocytes by abnormal cells.

Certain cases of acute lymphatic leukemia may present a history not unlike the case I have just shown you of idiopathic

purpura hemorrhagica, but the blood examination reveals leukemia, and the marrow at autopsy shows a crowding out of the megakaryocytes by the leukemic cells so that a secondary purpura hemorrhagica develops. A similar condition may exist with metastatic tumors, pernicious anemia, etc.

I now wish to show you another case of purpura that is not dependent upon reduction of the blood platelets or demonstrable alteration of any of the other elements of coagulation.

CASE 3.—The patient is a man, thirty-four years of age, who gives the following summarized history: A year and a half ago he had an attack of tonsillitis. Since then he has been well until five days ago, when he developed considerable pain with slight swelling and tenderness in his kness, then his ankles and elbows. Three days ago there developed all over his body except upon his hands and face a rash. The physical examination shows rather uniformly all over the body except upon the hands, face, and upper legs discrete purpuric macules and papules of from 2 to 5 mm. in diameter. The lesions are perhaps rather more marked about the joints. There are no deep ecchymoses, and no evidence of bleeding from the mucous membranes. The joints appear as he described them. The tonsils are enlarged and red. The heart is negative. The temperature is 101° F., the pulse 100; otherwise the physical examination is negative.

The laboratory examinations are negative, including a blood-culture, and a culture from a purpuric skin lesion which showed no growth. The blood examination shows that the platelets, bleeding time, coagulation time, and retraction of clot are normal. The red count and hemoglobin are normal. The white count is 8000 and the differential count essentially normal.

The case is one of purpura rheumatica, and although there are purpuric lesions on the skin, there are no hemorrhages from the mucous membranes, and there is no tendency to bleed, as occurs in purpura hemorrhagica. The reason for the purpuric skin lesions is unknown. I show you the case because one of the presenting symptoms is purpura and because the condition is to be sharply differentiated from purpura hemorrhagica.

Purpura rheumatica seems more closely related to cases of infectious arthritis than to the clear-cut types of hemorrhagic diseases. The joint symptoms are in all probability not due to hemorrhage into the joints. Purpura rheumatica appears like ordinary rheumatic fever plus purpura. There is, however, considerable evidence that the condition is not ordinary rheumatic fever, because the joint symptoms are usually mild, fever is often absent or slight and rarely high, and because endocarditis rather rarely occurs, and in clear-cut cases of rheumatic fever purpura is exceedingly rare. However, it would seem as if purpura rheumatica was due to some infection which produces a type of infectious arthritis, but one that may be different from that of rheumatic fever. The purpuric lesions are apt to recur in successive crops with or without the recurrence of the joint symptoms. The cases usually get well.

You will note that the blood findings in this as in other cases of purpura rheumatica are negative, which is in contrast to the findings in purpura hemorrhagica. Some cases of purpura rheumatica may develop, as do ordinary cases of rheumatic fever, a considerable secondary anemia, but this is not dependent upon hemorrhage, but presumably upon the toxemia. In such instances the platelets will often be found actually increased, as occurs so frequently in secondary anemia. Joint symptoms in purpura rheumatica are relatively prominent as compared to the purpura, and it is on account of these that the patient generally seeks relief and usually not especially for his purpura, which latter is the reason why the cases of purpura hemorrhagica seek relief. Also it is to be noted that joint symptoms usually do not occur in true purpura hemorrhagica.

In purpura hemorrhagica one never sees as extensive purpuric skin lesions as this case of purpura rheumatica presents without there being bleeding from the mucous membranes. It is perhaps unusual to have in purpura hemorrhagica such a generalized purpuric eruption as Case 2 presented. One not infrequently finds but a few scattered petechiæ as occurred in Case 1. However, many cases of purpura rheumatica do not have more than a few purpuric skin lesions, and if so, they are often sit-

uated in particularly one part of the body, perhaps especially about the joints.

Another point which has seemed to me to distinguish purpura rheumatica from purpura hemorrhagica is the character of the purpuric skin lesions. In purpura rheumatica the lesions have often seemed rather deeper in the skin and perhaps more sharply defined than the more superficial lesions of purpura hemorrhagica. Also the purpura rheumatica lesions often seem slightly elevated and are sometimes associated with urticaria and erythema, while the purpura hemorrhagica lesions are purely purpuric and are not elevated unless there is a large ecchymosis with a clot in the center. The differences between the lesions in these cases of purpura hemorrhagica (Case 2) and purpura rheumatica (Case 3) are difficult to describe, but I think that if you will compare the lesions in these two cases you will see that they have a different appearance.

The next and last case that I have to show you illustrates two points: (1) The early diagnosis of pernicious anemia, particularly from tongue symptoms—a condition originally described by William Hunter. (2) Symptomatic or secondary purpura hemorrhagica. I will present the case as it was two years ago and then show the patient to you as he is now.

Case 4.—Two years ago the patient, a man forty-four years of age, came to the hospital for relief of "burning of his tongue and sore mouth." The following is the only history of importance that he gave: He had always been well except for scarlet fever and measles as a child, and acute appendicitis, with removal of that organ ten years ago. About one to two months ago he noticed that he was slightly more tired than usual, but did not feel sick. He feels but little more tired now than one month ago. During the past two weeks he has been constantly bothered with a sore mouth and tongue, particularly along the sides and tip of his tongue, a sensation described as "raw"; a "burning feeling"; "as if he had taken acid."

The physical examination showed a well-developed man, weighing 148 pounds, perhaps slightly pale, with clear scleræ. The tongue appeared smooth, moist and shiny, rather beefy in

appearance, and with a few very small herpetic-like lesions along the sides. The mucosa of the mouth was, in general, reddened. The teeth were in very fair condition, but there was some definite though slight pyorrhea. Except for this the physical examination was entirely negative.

The blood showed: Hemoglobin, 90 per cent. Red count, 3,900,000. The red cells appeared at a glance not abnormal, but when critically studied one noticed that there was a slight variation in size and shape, with a general tendency to larger rather than smaller red cells, while very rarely there was to be found a definitely enlarged oval-shaped red cell well filled with hemoglobin, and at times a very small red cell. The white count was 5000. Differential count showed 72 per cent. of polymorphonuclear neutrophils, 21 per cent. of lymphocytes, 7 per cent. of other cells. The platelets as estimated by brilliant cresyl blue smears were slightly diminished. Other laboratory tests yielded no particular information except that there was no free hydrochloric acid in the stomach contents. (Tests for blood destruction were not done.)

To look at this man, at that time, you would not perhaps have thought that he had pernicious anemia, but with the history, the blood findings, and the anacidity taken together, the diagnosis becomes clear and is proved by what followed.

All cases of pernicious anemia do not have the tongue symptoms that this patient presented. About 35 per cent. of the cases have this symptom at some time in the course of the disease, and it is usually an early rather than a late symptom, and, not infrequently, the earliest symptom. However, it is often not as intense as this patient described, and often does not cause enough inconvenience for the patient to seek relief. It is important to remember that this is a rather characteristic symptom of pernicious anemia, and cases presenting such a symptom should have their blood critically examined. Of course, you must bear in mind other causes of sore mouth and tongue, as dental ulcer, syphilis, cancer, tuberculosis, infectious stomatitis, at times simple pyrrohea, hyperacidity, etc. The onset of pernicious anemia is usually notoriously insidious. General weakness, as

this patient presented in a mild degree, gastro-intestinal symptoms, of which this tongue symptom is one, or symptoms referable to the central nervous system, are usually the way the disease first manifests itself. At present most cases of pernicious anemia are diagnosed months after the disease starts, notwithstanding that the patient has consulted a doctor. This is, I think, because the disease is not thought of until the patient begins to look pale or yellow. By bearing in mind that adults over thirty years of age presenting tongue symptoms may be cases of pernicious anemia some cases ought to be diagnosed sooner than they are.

It is noteworthy that this patient had an absence of free hydrochloric acid in the stomach contents, as this is the usual finding in cases of pernicious anemia.

The patient looked "perhaps slightly pale," but the blood examination showed a diminished red count with high hemoglobin, that is, the blood exhibited a high color-index, which is so characteristic of pernicious anemia. The finding of a few large abnormally shaped red cells with a few microcytes in the blood of a person with as high a hemoglobin and red count as this patient had is very suggestive of pernicious anemia, though this diagnosis should never be made *solely* on the blood. It is not necessary to find blasts to make the diagnosis. It is difficult in certain cases of pernicious anemia at the height of a remission, and hence presumably in certain cases very early in the disease, to recognize perhaps any definite abnormality of the red cells, but with a critical examination some abnormality is usually observed. The white count and platelets are usually low in pernicious anemia, but may not be reduced or but slightly reduced early in the disease or when the patient is at the height of a remission. We have felt that the number of platelets has furnished us with perhaps the best single laboratory finding to tell us the state the bone-marrow is in in this disease, and thus aid us to determine the patient's condition.

Having digressed to point out the tongue symptoms of pernicious anemia which this case presented so well, I will show

you the patient as he is today, exhibiting secondary or symptomatic purpura hemorrhagica.

CASE 4 (Continued).—The tongue symptoms subsided about two weeks after the patient was first seen two years ago. Then in the following three months he gradually failed in health and became much weaker, paler, and lemon-tinted. He also suffered from mild gastro-intestinal symptoms. Following this relapse he gradually improved, so that he felt quite well seventeen months ago, but not as strong as formerly. He remained in this condition until six months ago. During these past six months he has very gradually grown weaker and has had occasionally a sore mouth, more or less continually indefinite gastro-intestinal symptoms, with at times diarrhea, and has looked pale and slightly yellowish. Four days ago he began to have slight bleeding from his gums, which has persisted, and tiny red spots appeared on his lower legs yesterday.

Physical examination today shows a very pale, slightly yellowish man, with numerous fine petechiæ in the gums and mucosa of the lower lip. Blood may be seen oozing from about several teeth. (The pyorrhea has been treated since he was first seen.) There are a few small petechiæ scattered over the lower legs. Except for a functional systolic murmur and a palpable liver, and a pale, somewhat atrophied, shiny, and smooth tongue the physical examination is entirely negative.

The blood (certain details noted will not be mentioned): At the time he had his first relapse the red count was 1,500,000, and the hemoglobin 45 per cent., the blood showing all the features of primary pernicious anemia, including a leukopenia, diminution of platelets, and the presence of megaloblasts. Today the red count is 1,000,000, hemoglobin 35 per cent.; blasts are very rarely seen. The red cells show considerable variation in size and shape, and large oval and pear-shaped, deeply staining red cells occur. However, there is not as great a degree of variation in the size and shape of the red cells as occurred during the first relapse or as much as one might expect with this degree of anemia. This perhaps suggests an exhaustion of the marrow. Also the reticulated red cells are unusually low—but 0.3 per

cent.—which under the given circumstances also clearly suggests exhaustion of the marrow. One usually finds a slight increase of these cells in pernicious anemia, 2 or 3 per cent., and at times of rapid marrow activity they may reach as much as even 45 per cent., and often 10 per cent. The white count is 2000, and the differential count shows 65 per cent. of small lymphocytes, and but 30 per cent. of polymorphonuclears. Thus we find a marked absolute decrease of the white cells originating in the marrow, which further suggests a severely depressed activity or exhaustion of the marrow. The platelets are scant and number about 70,000, further suggesting a depressed or exhausted state of the marrow. The bleeding time is slightly prolonged, the coagulation time normal, and the clot retracts but very slightly. The development of the purpura hemorrhagica in this case of primary pernicious anemia illustrates an instance of secondary or symptomatic purpura hemorrhagica. What has occurred is that with the depressed or exhausted marrow activity the platelets have fallen so low that purpura hemorrhagica ensues. The marrow exhaustion is evidenced in the blood by not only one of the three formed elements, originating in the marrow, but by all. Pathologically the marrow of this patient would probably not show fatty degeneration (a soft yellow marrow) as occurs in idiopathic aplastic anemia, though this may be found as a terminal event in pernicious anemia. Probably in this case the marrow would be reddish and show an increase of erythrogenic tissue of abnormal character displacing and thus causing diminution of the megakaryocytes and normal leukoblastic tissue, though this latter tissue may be actually increased, but of an abnormal type. At all events the physiologic activity of the marrow becomes so weakened that it is unable to functionate to produce in the circulation more than a few of the normal elements. The development of purpura hemorrhagica in pernicious anemia, even though it be only manifested by a slight oozing of the gums, is a serious symptom. It rarely becomes marked, and by no manner of means do all cases of pernicious anemia have this symptom. It usually signifies that the disease has run its course and that a remission will not occur spontaneously nor can it be produced,

though the patient may continue to live for some weeks or months. However, a few cases may perhaps have this symptom and later have a fair remission.

There are numerous things about purpuras and hemorrhagic conditions as well as about the early symptoms of pernicious anemia that I have not told you about, but I have tried to point out some of the important things.

Treatment.—In regard to the special treatment of purpura hemorrhagica, whether it be primary or secondary, I will have time to say but a word. There is no special treatment unless the cases are having considerable hemorrhage, and then the best treatment is to give intravenously a suitable amount of whole blood from a donor of the same iso-agglutination group as that of the patient. This should be done as early as possible in the acute idiopathic cases. Unless the transfusion causes in some manner a permanent rise in the patient's platelets the cessation of hemorrhage will usually last about as long as the life of the transfused platelets, that is, about three to five days, though in some instances a rapid destruction of such platelets seems to occur, and the effect is then even shorter. Probably all the beneficial effect is not referable to the transfused platelets. A permanent or marked temporary rise of the platelets following transfusion in purpura hemorrhagica is referable to a stimulation, direct or indirect, of the patient's platelet-forming elements, or to a prevention of a destruction of the patient's platelets. Repeated transfusions are often without any lasting effect. In the instances where a toxin is recognized and removed, as in benzol poisoning, repeated transfusions are especially indicated so as to temporarily keep the patient from bleeding and to give the marrow time to regenerate and so recovery to occur. Serum at times may perhaps have some influence upon cases of purpura hemorrhagica, but is certainly not as effective as whole blood. Neither transfusion nor serums seem to have any particular influence on the purpuric skin lesions in purpura rheumatica, nor could we reasonably expect that they would, as in this condition there is no clear-cut recognized abnormality of the blood-coagulation mechanism.

The next best treatment to transfusion is the use of thromboplastic preparations derived from fresh tissue juice, perhaps combined with thrombin preparations. Tissue juice accelerates the coagulation of the blood markedly as well as do the platelets. This action of tissue juice has been recognized for years, but it has been but occasionally used for therapeutic purposes until recently. With Howell's discovery that certain extracts of the brain having the property of kephalin exert a marked thromboplastic action, it has been quite simple to obtain from animals stable, concentrated, and active preparations for local, subcutaneous, and intravenous use. The use of such substances is in the experimental stage, but seems to promise favorable results. Such preparations may be used before transfusion or when bleeding is slight, or they may be given trial at any time, but it is to be remembered that whole blood is at present the most logical and best therapeutic agent for the control of bleeding in pathologic hemorrhage.

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AMEBIC DYSENTERY AND ASSOCIATED CONDITIONS

General Consideration of the Amebæ Occurring in Man; Discussion of Varieties of Entamebæ; Discussion of Cases; Symptomatology; Diagnosis Based on Laboratory Evidence; Full Discussion of Treatment and Use of Emetine; Complications and Sequelæ; Differential Diagnosis; Bibliography.

October 27, 1917.

FOR consideration this morning we have two patients, one of whom is a typical and comparatively early case of amebic dysentery; the other presents symptoms which conform clinically to the picture of this same disease after the lapse of a number of years. In the first patient the diagnosis of his disease and its etiology are well understood; a specific treatment is available, and the prognosis is, comparatively speaking, extremely satisfactory. In the second case the primary etiologic factor is still undetermined and an accurate diagnosis has not been reached, although a thorough investigation has been made by clinical and laboratory methods. The condition is highly refractory to therapeutic measures and the prognosis is extremely unfavorable.

General Consideration of the Amebæ Occurring in Man.—In order to diagnose these cases it is necessary to understand thoroughly the amebæ which may be encountered in the alimentary tract in man. There are but three—the two parasitic entamebæ, namely, histolytica and coli, and the non-parasitic forms known as the limax group. The term "limax" includes a considerable number of species many of which have been only very incompletely described. They would be of no interest in clinical med-

THE AMEBÆ FOUND IN THE ALIMENTARY CANAL IN MAN

Variety of ameba.	Microscopic examination.	Morphology.		Cultural examination.	Parasitism in man.	Pathogenicity in man.	Transmission to lower animals.	Effect of emetine.
		Trophozoites.	Cysts (usual number of nuclei).					
E. histolytica.	Found in feces and in tissues of body.	Evidences of active motility, phagocytosis, pseudopodia of clear ectoplasm.	4	Negative.	+	+	+	Highly amebicidal.
E. coli.	Found in feces.	Homogeneous granular protoplasm very sluggish.	8	Negative.	+	o	+(?)	?
E. buccalis.	Found especially around the gums.	Small ameba tending toward histolytica type.	?	Negative.	+	o(?)	o	Amebicidal.
Limax Group.	Not demonstrable microscopically.	Variable according to species.	1 or 2	Easily cultivated.	o	o	o	Amebicidal *in vitro.*

icine except for the enormous confusion which they have caused in being mistaken for the pathogenic amebæ. They are not parasitic and cannot even multiply in the intestinal tract. Consequently they are not seen upon microscopic examination of the feces, but they can be demonstrated by cultural methods.

As regards even the principal characteristics of the amebæ found in man it must be noted that the literature is in an extremely unsatisfactory condition. Many contradictory opinions have been advanced concerning fundamental features, such as the number of pathogenic species occurring in the intestinal tract and the question of their cultivation on artificial media. In the last few years these opinions are gradually being harmonized. The data presented in the outline (p. 1126) conform to the generally accepted views of the best American and European authorities.

In this outline *Entameba tetragena* is not mentioned. It was described by Viereck in 1907 as a common cause of amebic dysentery in man and as a species distinct from *E. histolytica*. Careful descriptions were given of the characteristics of the trophozoites of the two species. The principal difference, however, was found in the propagative stage, *E. tetragena* producing four-nucleated cysts, whereas *E. histolytica*, according to Schaudinn, produces resistant forms by pinching off small pieces of protoplasm somewhat after the manner of budding in yeast cells. The establishment of this new species was soon recognized throughout the world. However, in 1911 Dr. Walker, formerly of Dr. Theobald Smith's department, decided that the normal manner of propagation in *E. histolytica* is not through a process of budding, but by the formation of a four-nucleated cyst. After careful study Walker finally concluded that *E. histolytica* and *E. tetragena* are identical. This apparently radical view was soon generally accepted throughout Europe and America, and the name *E. tetragena* has been dropped, *E. histolytica* having priority.

The attempts at cultivation of the entamebæ are full of interest. If a dysenteric stool rich in amebæ is inoculated on a medium containing only agar and water, an abundant growth

of amebæ frequently appears after one or two days. In general appearances the amebæ are not unlike those which were inoculated. Moreover, if this culture is inoculated in a monkey, amebic dysentery may occasionally be reproduced. On closer examination these amebæ have always proved to be of the limax group, having been ingested accidentally in the food and drink. Direct experimental evidence under carefully controlled conditions shows that they are non-pathogenic for man and lower animals and they cannot even colonize in the intestinal tract. The occasional production of dysentery by the inoculation of a freshly isolated culture may be accounted for by the mechanical carrying over of a few pathogenic cysts or perhaps by the spontaneous development of a natural infection of dysentery. The chief dissenters from this view are Musgrave and Williams. There is, of course, no inherent characteristic of the entamebæ which would prevent their cultivation. Indeed, there is every reason to believe that this will some day be satisfactorily accomplished.

The morphology of the amebæ has already been fully considered in your course in protozoölogy. Suffice it to say that in borderline cases the distinction beween the vegetative stages of coli and histolytica is an extremely difficult one. The study of the encysted stage is often disappointing. The cysts are frequently rare or absent altogether. There is no known way of making the trophozoites encyst *in vitro* or *in vivo*. Moreover, the number of nuclei is not absolutely fixed. Thus it is possible for cysts of *E. histolytica* to have two, four, six, or eight nuclei or even three, five, or seven. Similarly, *E. coli* may produce cysts containing four, eight, twelve, sixteen, or even more nuclei.

For the sake of completeness I have also included *E. buccalis* in this outline. Its position as a species cannot be fully determined till its propagative stage is known. I have indicated that it is non-pathogenic, though it may at times be one of the secondary factors in pyorrhea alveolaris.

Discussion of Cases.—In this first patient the essential features of his record are as follows:

CASE 1.—M. J., Hospital number 218,247, male, sixty-two years old, by occupation an artist.

Family History.—One sister died of tuberculosis at the age of twenty-five years; otherwise there is nothing important.

Past History.—This is essentially negative. The patient has never been robust and has always had "to take good care of himself."

Present Illness.—In May of this year—*i. e.*, about six months ago—the patient while in the West Indies had a sudden attack of diarrhea, passing three to five stools per day. Microscopic examination showed the presence of amebæ, and treatment with emetine instituted one month after the onset produced prompt relief, the patient remaining in relatively good health for about four months. Then a somewhat gradual onset of "diarrhea" occurred, culminating in a typical relapse. The patient does not know whether the stools contained any blood, as he did not notice their character.

Physical examination reveals nothing remarkable. The patient is not well nourished; there is moderate secondary anemia. The liver dulness is not increased and the edge is not palpable. There is no definite tenderness over the colon, and the sigmoid is not palpable.

Special Examinations.—A fresh specmen of stool shows a small amount of blood and several amebæ in both the motile and the encysted stage. Both stages show the usual characteristics of the pathogenic amebæ. In order to specify these organisms exactly they should be called *Entameba histolytica*, signifying a parasitic organism which dissolves tissues. The diagnosis of the disease is *amebic dysentery*. It is not necessary to use the term *entamebic dysentery*. A more precise designation would be *intestinal amebiasis;* this also has the advantage of conforming with such terminology as *filariasis* and *trypanosomiasis*.

Symptomatology.—In this one patient we have represented both the acute and the gradual types of onset. Many cases begin without any premonitory warnings recognized by the patient. Frequently, however, vague feelings of abdominal discomfort may be present for weeks or months, but they may not attract

the patient's attention. Examination of the stool at this period frequently reveals the true diagnosis. If untreated the infection may lie dormant for long periods before the acute attack develops or, less commonly, it may terminate in recovery.

The distinction between diarrhea and dysentery is one of considerable importance, and the terms are too often used indiscriminately. The information given by the patient is usually without value or even very misleading. It is a very common thing to be told that the movements contain no blood at all, but are very watery, though the first examination may reveal gross clots of fresh blood. Mistakes in the opposite direction are much less common. In this particular instance we are more fortunate; the patient admits that he does not know the character of his stools, never having noticed them. This is a very unusual answer.

If this case were allowed to go untreated the chances are that after some weeks of discomfort the symptoms would eventually subside and recovery would apparently have taken place. After a few weeks or months another relapse could be confidently expected. In taking the history of a case of dysentery it is extremely important to determine carefully whether there has been a succession of acute exacerbations followed by periods of remission or even constipation. Such a history is extremely suggestive of dysentery of the amebic type regardless of whether the remissions have occurred spontaneously or in response to emetine or any other form of therapy.

Clinically, there is but little to depend on for the differentiation of the bacillary and the amebic types of infection. The former tends to run a more acute course, the temperature being higher, and the patients look and feel very ill; in unfavorable cases evidences of peritonitis may appear. In the long-standing cases involvement of the liver, of course, indicates an amebic infection.

Evidence.—The ultimate diagnosis rests with the microscopic examination of the stools. The amebæ are not always abundant, since the early lesions are frequently situated high in the bowel in the cecum and ascending colon. In such cases a saline purge is

necessary to obtain suitable material for examination. The practice of passing a rectal tube or giving an enema is not to be recommended. Also the use of castor oil is inadvisable, since the many droplets of oil in the microscopic field causes momentary delay in the search for cysts. If a free purgation is obtained with magnesium sulphate, not only the first specimen but also the second and third should be carefully examined. It is of vital importance that only a few minutes should elapse before the examination is commenced. If some delay is unavoidable, the material may be kept either at room temperature or at 37° C. The organisms become more sluggish at the lower temperature, but they remain viable even longer than in the incubator. After a delay of three or four hours specimens frequently become quite useless.

Small flakes of blood or mucus should be selected, and if none are seen, shreds of mucus can often be obtained by whipping the stool with a platinum wire. It is often advised that the criterion of motility is essential in the identification of amebæ. However, it is entirely possible to recognize non-motile and pre-encysting forms with certainty. Indeed, if motility is required, diagnoses will frequently be missed even though the examination is made with an adequate warm stage; moreover, some of the pus cells may occasionally show slight ameboid motion.

After establishing the presence of amebæ it is theoretically necessary to identify the species and prove their pathogenicity. In an outspoken dysentery the amebæ if present are ordinarily characteristic of *E. histolytica*, and the final diagnosis is simple. Hypothetically it would be possible to have typical symptoms and only *E. coli* present in the stools. Fortunately this combination, if it occurs at all, is exceedingly rare. I have seen some moderately active cases whose stools contained amebæ which in their morphology tended more toward the coli than toward the histolytica type. These cases, however, responded promptly to emetine. Therefore when slight dysentery or even persistent diarrhea is present accompanied by amebæ in the stools, it would from a clinical standpoint be extremely unsafe to reject the diagnosis of amebic dysentery. There is another group of

cases in which the decision is more difficult; namely, when amebæ are found in the stools in the absence of any clinical symptoms, past or present. I know of one such instance in which after the examination of many specimens in the laboratory the amebæ were identified as *E. coli*. The patient was given a good prognosis and was not treated. A few months later a typical and fatal attack of dysentery developed. It is possible that the amebæ were incorrectly identified, for even the presence of an occasional eight-nucleated cyst does not absolutely establish the species as *E. coli*. On the other hand, in addition to the presence of *E. coli*, there may have been a latent infection of *E. histolytica*. Unfortunately, therefore, a perfect identification of species by a protozoölogist does not permit of a final clinical diagnosis. The establishment of the presence of *E. coli* does not exclude the possibility of the existence of a mixed infection.

In the case of liver involvement it is not an uncommon procedure to puncture a suspected abscess for the purpose of diagnosis. Pus from such abscesses usually does not contain amebæ, and bacteria are generally present. Even though the danger is slight, there is always the possibility of spreading the bacterial infection. After a surgical operation the pus which drains from these cases usually does not contain amebæ until several days have elapsed, *i. e.*, until the necrotic walls of the abscess begin to slough away. In the infectious diseases it would seem to be a fairly general law that the inciting organisms are found less frequently in the contents of a cavity and most abundantly in its walls, for this represents the site of the active process.

Therapy.—This morning we shall have time to consider only the specific measures. Intramuscular injections of emetine have replaced all previous forms of treatment. A soluble salt of emetine, such as the hydrochlorid, must be used. A good routine is to inject 1 grain morning and evening for one or two days, and continue with 1 grain in the evening for twelve to fourteen days. Then, after having discontinued treatment for two to four weeks, it is advisable, as a precautionary measure, to give a second course consisting of 1 grain intramuscularly per day for two weeks. This second course of emetine could hardly be as

effective as the treatment of a relapse, since amebæ in the encysted stage are probably not injured by therapeutic doses of emetine. The immediate relief of symptoms is so prompt and so complete that it is seldom necessary to employ subsidiary measures, such as the use of Dover's powder. Usually after about two days the stools will be semiformed or even formed, the blood will have disappeared almost completely, though a few amebæ may still persist. Although the immediate response is so excellent, it is almost the rule in these cases that a typical relapse will occur after a few months or even years. I have in mind one patient, a native of Massachusetts, who contracted the disease in Central America. He was treated energetically with emetine and apparently cured, remaining perfectly free from symptoms for three years. Then, without having revisited the tropics and without being re-exposed to infection in any known way, a perfectly typical relapse developed. This yielded promptly to emetine, only to be succeeded after three months by another relapse. This seems discouraging. However, if each relapse is promptly and thoroughly treated these patients will eventually recover.

This general routine for the use of emetine can only be applied in the ordinary typical attack. There are two groups of amebic cases in which emetine is almost without action—namely, (1) the extremely acute, and (2) the extremely chronic types. In fulminating infections the use of as much as 2 grains of emetine intravenously at one injection frequently fails to control the symptoms, and the patients go on to a rapidly fatal termination. It is probable that death in these cases is due to a secondary bacteremia, though the proof for this view is not yet complete. Indeed, like the other protozoa and in contrast to many of the pathogenic bacteria, it is not known in what way the entamebæ produce their harmful effects. It may be seriously questioned whether *E. histolytica per se* is able to produce a fatal disease in man; in the majority of instances the fatal termination is apparently effected only by the aid of secondary bacterial infection.

No explanation is at hand for the failure of emetine in the

extremely chronic cases. I have studied several such cases with Dr. Baetjer in Baltimore. They were characterized by a watery diarrhea with only the occasional appearance of traces of blood and mucus. From the morphology alone the pathogenicity of the amebæ found in the stools might well have been seriously questioned; their etiologic rôle, however, was proved by animal experimentation. So you must not allow the failure of emetine in chronic cases to deter you from a final diagnosis of amebic infection.

The history of the development of therapy with ipecac and emetine has been an interesting one. The crude drug had long enjoyed considerable popularity with the natives of India. These clinical results attracted but little attention in the western world. The drug was still further discredited by apparently careful work, which seemingly proved that any virtue which it possessed was at least not due to its content in emetine. Equally good results were obtained when de-emetinized preparations were substituted for the crude drug. It was hoped that this apparently reliable discovery would greatly increase the use of ipecac since the successful administration of emetine by mouth is an extremely tedious process. However, both the crude ipecac and the de-emetinized preparations fell into disuse. Vedder in 1910 showed that emetine was highly amebicidal *in vitro* for cultural amebæ, and a little later Rogers introduced the use of the alkaloid in India. Recently the use of emetine has supplanted not only the crude ipecac but also the custom of giving cleansing irrigations—in the ordinary cases rectal irrigations of saline or of highly diluted solutions of quinine are no longer employed.

There are certain precautions which should be observed in the use of emetine. It has been reported that untoward effects sometimes appear shortly after the first injections of the drug. The initial symptoms which have been described are hyperesthesia, paresthesia, and other disturbances of sensation, especially of the lower extremities. If these appear, the injections should be discontinued for a time at least. Such symptoms may be due to an unusual susceptibility or to the unexplained appearance of toxic properties in apparently standard preparations of emetine.

The latter feature has been emphasized in the literature, but, unfortunately, sufficient care has not always been exercised in distinguishing between the supposedly toxic properties of emetine and some of the less common manifestations of the amebic infection itself.

There is another point of considerable practical importance concerning the injections. The drug is rather irritating and not only routine but even expert care in asepsis must be exercised if secondary infection is to be always avoided. The injections should be given intramuscularly, and they should not be repeated in the same location until a period of several days or a week has elapsed.

One other drug should be mentioned, for it may possibly prove to be as good or possibly better than emetine. This is a small shrub growing in northern Mexico and Texas. Botanically it is one of the simarubaceæ; locally it is known as chapparo amargoso, a Mexican designation signifying "bitter bush." It has been used for decades by the Mexicans with such good results that it has been adopted for routine use by some of the American practitioners in Texas. The best accounts have been reported by Nixon. An infusion about the color of weak tea is prepared with boiling water from the dried stems and leaves of the plant. This is apparently non-toxic for man and is administered in liberal quantities by mouth and by rectal injection. The immediate results are as good as with emetine and the relapses are much less common.

Our rather limited experience here in the North with this plant has been encouraging in the typical cases. In two of these the immediate response was very good. A third case was particularly interesting. This patient after receiving injections of emetine for two weeks still had dysentery with motile amebæ in the stools. He yielded promptly to treatment with chapparo. Clinical evidence, even though very encouraging, can be notoriously misleading. Recently some additional information concerning this plant has been obtained by Dr. McIver and myself.[1] We have secured concentrated aqueous extracts which proved to

[1] Publication in press.

be highly toxic for small animals. A feasible method was devised for isolating this toxic principle in relatively pure form. Chemically the reactions of this purified product are interesting; it gives a fair precipitate with some of the more general alkaloidal reagents; with sulfuric acid a striking color reaction is produced, and after boiling with hydrochloric acid it reduces Fehling's solution. This product is amebicidal *in vitro*. Two cases of amebic dysentery yielded promptly to small doses of this product administered by mouth. It is needless to say that its ultimate value can only be determined by the observation of a large series of cases over a period of several years.

Complications and Sequelæ.—One can with reasonable confidence expect to avoid complications or sequelæ in amebic infections under proper treatment. Indeed, after definite signs of liver abscess have already developed complete relief can sometimes be obtained by emetine therapy without resort to surgical interference. Metastatic abscesses from the intestines by way of the blood-stream naturally localize first in the liver. The right lobe being larger than the left, a proportionally large number occur on the right side. They may be single or multiple and occasionally they are surgically inoperable. Not infrequently in a patient with definite clinical signs of liver abscess nothing will be found on exploration. It is quite possible to overlook these abscesses surgically; the lesion may be very small and situated high up in the dome of the liver, or it may be a larger mass of necrotic tissue containing no free fluid. In such cases it is important to examine any tissue obtained in the lumen of the aspirating needle.

A liver abscess may rupture into any of the adjacent structures, such as the lung, so that the diagnosis has been made from the resulting sputum that is coughed up. Exceptionally, as a curiosity, the primary abscess may appear in other organs of the body, such as the brain or the spleen.

In considering the pathogenicity of the amebæ a remarkable feature has been pointed out by Dr. Edsall, namely, that although relapses are extremely common in the intestinal infections, they are rare indeed in the cases of liver abscess. This was true of

the hepatic infections even before the introduction of emetine. Once a case has been explored surgically and recovery has taken place then relapses seldom, if ever, occur.

The cases of amebic infection will not always conform to simple well-recognized types. A few years ago a boy of about fourteen years came to the hospital presenting anatomically a typical picture of Hirschsprung's disease. Examination of the stools showed the presence of pathogenic amebæ, and upon inquiring more carefully into the history it developed that there had been a chronic dysentery of many years' standing. At operation a fibrous band was found just above the sigmoid. The healing of the lesions in the submucosa of the intestine had led to excessive scar formation and the development of a moderate grade of stricture.

A rare and extremely unfortunate occurrence is the development of a polyarthritis after amebic dysentery. Its origin is unknown; possibly it results from a secondary bacterial invasion of the blood-stream.

Like many other protozoan diseases, the carrier stage is a well-recognized condition, and is one of the important ways in which the infection is propagated. I have seen one individual who had always been free from symptoms but whose stools usually contained an abundance of four-nucleated cysts; these were proved to be pathogenic for animals. In contrast to these quiescent cases there is another very different type of long-standing infection, namely, chronic amebic dysentery. Some of the late cases could very properly be regarded as illustrations of the sequelæ of the disease; in many of these patients it eventually becomes difficult or impossible to demonstrate amebæ, and the essential lesion is an extensive involvement of the colon by pyogenic bacteria.

We have such a case here in the wards now. This man, fifty-two years old, was formerly a fisherman in Nova Scotia. He has been in Massachusetts two years. Two months ago he was admitted to the emergency ward in almost complete collapse with an increase in pulse, respiration, and temperature (pulse, 100; respirations, 25; temperature, 100° F.). Apparently he

had lost considerable blood by hemorrhage from the rectum. He was incontinent and was passing small quantities of blood and pus more or less continuously. Some days later the following notes were obtained:

Family History.—There has been considerable exposure to tuberculosis, the mother and one sister having died of this disease.

Past History.—The patient says that he has a cough every winter and that he had one hemoptysis five years ago, spitting up a tablespoonful of blood. Otherwise the past history is negative, though rather indefinite and unsatisfactory.

Present Illness.—For the past nineteen summers the patient says he has had attacks of "diarrhea" similar to the present one. This one seems to have come on without much warning.

Physical Examination.—There is some spasm and some tenderness over the transverse colon. The liver dulness is not increased, the edge is not palpable, and there is no tenderness along the costal margin.

Special Examinations.—The blood showed on admission a slight secondary anemia. The white count was 27,000, showing a polymorphonuclear increase. The Wassermann reaction was negative. Dr. Taylor found that the patient's serum agglutinated a culture of the Strong variety of bacillary dysentery at a dilution of 1 : 50. The stools were composed of blood and pus with virtually no fecal matter. No animal parasites were found; no amebæ were seen either in the motile or encysted stage. Examinations for tubercle bacilli were negative. Cultures for the organisms of bacillary dysentery were negative. Practically complete absence of the colon bacillus from the stools was noted.

Differential Diagnosis.—In this patient we can pass at once from the non-infectious diarrheas and proceed to the infectious diseases. We must consider not only the two specific dysenteries but also all of the other conditions which may simulate these two diseases. Especial attention should be directed to syphilis, to tuberculosis, and to malignancy of the large bowel. You will not, of course, overlook the possibility of hemorrhoids. The

symptoms in this man have been much more acute than are characteristic of syphilitic proctitis. The history directs attention to tuberculosis, but the general and special examinations show no evidence of active tuberculosis anywhere in the intestines or in any other part of the body. Malignancy is an extremely important consideration, and the differentiation from dysentery is not easy. I have seen mistakes made in both directions, and these happened after the cases had been carefully studied. One patient with a moderately large mass over the descending colon was regarded for some time as an amebic infection. The condition was eventually proved to be a carcinoma. Another case of intermittent dysentery eventually came to operation. The stools had been free from amebæ and at exploration the diagnosis of diffuse carcinomatosis was made. A section of the bowel was removed and amebæ were demonstrated in the submucosa.

In this patient I think we can with reasonable safety exclude syphilis, tuberculosis, and malignancy. While these conditions may simulate a short attack of typical dysentery, it is only the amebic and bacillary infections that can produce severe, sustained symptoms extending over months and years; however, in their atypical forms either of these varieties may simulate perfectly the usual course, for example, of tuberculosis of the intestine. In this patient it is now impossible to determine whether the disease in its origin some years ago was a bacillary or amebic infection. The agglutination tests are somewhat suggestive, but unfortunately these tests as well as the cultural procedures have never been fully developed for use in chronic colitis. In order to explain these dysenteries it is not necessary to postulate a new specific etiologic agent. There is considerable evidence that both amebic and bacillary dysentery are endemic in New England. Indeed, acute bacillary infections occur with considerable frequency in children in the summer months. On the other hand, it does not necessarily follow that these cases will conform to the known types; it is quite possible that still another specific agent of dysentery may be found. The ultimate solution of the problem would be greatly facili-

tated by the application of cultural methods based on the new principles that have recently been developed by Dr. Teague in the isolation of the typhoid bacillus from the stool.

The treatment of these neglected cases is very unsatisfactory. Even if amebæ could be demonstrated, virtually no benefit could be expected from emetine. Consequently, its administration on general principles is not indicated. Similarly, it is too late for the use of the various specific sera that have been proposed for the treatment of bacillary infections. One must resort to general measures, giving attention to the comfort of the patient, the diet, the minor measures for the control of hemorrhage; fluid must be restored, if necessary, by the injections of salt solution or by the transfusion of blood. The intestinal discomfort can be relieved symptomatically by the use of bismuth or opium. Surgical interference has been practised lately in many of these cases. Ordinarily an appendicostomy is done to facilitate the irrigation of the large bowel. It is permissible to use with care mild cleansing solutions, such as normal saline solution or highly diluted quinine (1 : 5000). The irritating solutions have never come into general use, and in my opinion they should be carefully avoided. In advanced cases the results of operation are too often discouraging.

Recenty some success seems to have been obtained by performing an ileostomy. By means of this artificial anus the large bowel is put to rest and its irrigation is facilitated. The operation together with the resulting rapid passage of the intestinal contents through the small bowel constitutes a considerable tax on the individual's strength. The surgeons feel that frequently interference is delayed too long and that it is employed only as a last resort in subjects already much emaciated. In moderately early cases medical measures should first be given a thorough trial; if the symptoms do not yield after a reasonable interval, then surgical procedures should be seriously considered.

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FOCAL TRANSVERSE LESIONS OF THE SPINAL CORD

Definition. Importance of Early Recognition of Etiologic Factor on Account of Great Variety of Treatment. Possibility of Making Such Diagnosis Should be Possible in Most Cases by Elimination and Proper Employment of Modern Methods in Diagnosis, Particularly Examination of the Spinal Fluid.

IT is often easy, but frequently difficult, to diagnosticate a focal transverse lesion of the spinal cord. The importance of making a correct and early diagnosis in such a condition is great, because the treatment is so various.

What is meant by the term "focal transverse lesion of the spinal cord"? Simply speaking, any affection which, acting at a given level of the cord, prevents or impairs the passage of nerve impulses above and below this segment. Why, you will say, is not the time-honored term "transverse myelitis" employed, for that is obviously what you mean? Because the term "myelitis" is a poor one, connoting inflammation, and most of the lesions with which we are here concerned are non-inflammatory. While the initiated may use this short expressive term without risk, there is, as I have found, danger of misguidance from the employment of "transverse myelitis" when applied to tumors, hemorrhage, and fractures, all of which are frequent factors in the symptomatology of focal lesions of the spinal cord.

As has been said, many focal cord lesions are easy of diagnosis, as, for example, the considerable group of fractured spine. Of those diagnosticated with difficulty, the chief stumbling-blocks

are the tract or system diseases, certain disseminated cord lesions, and affections of the peripheral nervous system.

What, then, are the characteristics by which a transverse lesion of the cord may be recognized, and what the differentiating points from conditions which simulate it? Typically, a focal transverse lesion, if not too sudden in origin nor too complete in its effects, will show (*e. g.*, a tumor pressing upon the middorsal cord) ataxia and spasticity of legs, together with diminished cutaneous sensibility up to the affected level, in this case the ensiform cartilage. Above this level there will be a band of hyperesthesia 2 to 4 cm. in width. Above this, motor and sensory functions intact. To this picture may be added in many cases pain affecting the sensory nerve-roots of the level affected, and rarely atrophy of muscles supplied by the motor nerves of this same segment. If under observation for some time, we usually find an increase in severity of the above symptoms, but do not expect evidence of much vertical extension of the process.

In what manner does a *tract* or *system disease* differ from this description? Syphilitic ataxic paraplegia, combined system disease, and, rarely, tabes may be mistaken for focal disorder of the cord. In all the presence of a well-marked level of sensory change and localized root pain (confined to a given level) are absent; and in the two latter observation over a period of time will show unmistakable signs of involvement of the cord at more than one level.

Disseminated lesions of the cord are usually manifest by their multiple foci. Nevertheless the lesions of multiple sclerosis and syringomyelia may be so much more marked in a given segment that the other lesions of the cord and even brain may be overlooked. Even on the advice of careful neurologists operation for supposed cord tumor has frequently been performed in such diseases.

Diseases of the peripheral nervous system are not infrequently confused with cord lesions, but this statement applies more to the tract than to focal disorders. In these cases we do find sensory changes, but even superficial examination reveals a diminishing

anesthesia from periphery to center, and fails to show a proper sensory level; moreover, spasticity is absent.

It is then a comparatively easy matter to separate the typical focal cord lesions from other lesions. Difficulty arises when we are concerned with the atypical of either group. Not less in importance and no easier is the recognition of the several causes and pathologic states within the group of focal lesions.

Before we consider cases it will be best to speak of *accessory aids to diagnosis* which are now available. From examination of the blood we may derive knowledge of some benefit. A leukocytosis will suggest infection, and perhaps lead to detection of abscess, as in two of our cases. Pernicious anemia may be detected and thereby throw the evidence of a questionable case in favor of combined system disease. A positive blood Wassermann must be explained, but with the reiterated warning of the argument that because (1) the patient has spinal cord trouble, and (2) the patient has a positive Wassermann, *ergo*, the patient must have syphilis of the spinal cord. From the urine less is to be learned than in many disorders. The occurrence of Bence-Jones bodies, however, should be noted in connection with myeloma of the vertebræ.

Of greater value than the above is the *x*-ray. The field of the *x*-ray is here limited—from the diagnostic point of view—to affections of the vertebræ; only by inference can we estimate the effect of fracture, dislocation, or disease of the vertebræ upon the spinal cord.

By far the most important laboratory aid is that presented by the examination of the spinal fluid. The greater number of focal cord lesions are produced by pressure exerted from within or without the cord; this results, as Mestrezat[1] first pointed out, in the formation of a culdesac below the point of compression and a dilatation of the blood-vessels at the point of pressure. Therefore on withdrawal of spinal fluid from below we find it under low pressure and very rich in albumin and frequently of a clear yellow color. Moreover, this lemon-colored fluid quickly clots. Cells are absent or few in number and cultures are negative. The

[1] Mestrezat: Liquide céphalo-rachidien normal et pathologique, Paris, 1912.

low pressure is best explained by the shutting off of this culdesac from the spinal fluid column above the compression, spinal fluid pressure corresponding chiefly to the venous pressure in the brain; owing to dilatation of veins (usually visible at operations on such cases) transudation into this area of low pressure readily takes place, giving a high albumin content and allowing thrombin and thrombinogen also to pass, along with coloring-matter, presumably from decomposed red blood-cells. The usual absence of cells and constant absence of bacteria signify that the formation of this fluid, characteristic of cord compression, is not of inflammatory origin.

As variations of this "syndrome of Froin"[1] we find at times that there is an increase of inflammatory cells, usually lymphocytes, signifying that besides the compression there is inflammation present. At other times the pressure is not low. But the most important variation gives us a fluid which superficially seems to have no relation to the "complete syndrome" as given. Where presumably the pressure upon the cord has been insufficient to shut off the spinal fluid column, we find a fluid of normal appearance, colorless, under normal pressure, but one which contains an abundance of albumin. This fluid does not clot, it may or may not contain cells. Such a fluid falls into the group of "Nonne's incomplete syndrome."[2] The significance of both fluids is the same—*i. e.*, compression of the cord.

Unfortunately, the spinal fluid findings do not tell us where or what the lesion is, though it is noticeable that the more complete the compression and the more rapidly it has been produced, and also the further down the cord the compression exists, in these cases the complete syndrome is more likely to occur.[3]

Unfortunately, also, the findings are not always characteristic of cord compression where such exists; but the existence of the incomplete syndrome is evidence in favor of it; the presence of the complete syndrome is perhaps as nearly pathognomonic as any single sign in medicine.

[1] Froin: Gaz. des Hôp., 1903, lxxvi, 1005.
[2] Nonne: Deutsch. Ztsch. f. Nerven., 1910, xl, 161.
[3] Ayer and Viets: Jour. Amer. Med. Assoc., 1916, lxvii, 1707.

Let me now place before you a list containing at least all the common, and some unusual, types of focal cord disorder. The following classification alone, giving conditions only which are known to me personally, gives a good idea of the great variety of pathologic agents at work and of the manner in which the spinal cord may be attacked at a given level, presenting the clinical picture of "transverse myelitis."

Intramedullary affections:

Hemorrhage.
Myelitis—infectious or toxic.
"Myelitis"—vascular thrombotic.
Tumor—glioma.
Syringomyelia—gliosis spinalis.
Dermoid cysts and growths from ependyma of central canal.
Solitary tubercle.

Meningeal:

Chronic meningitis (more often meningomyelitis), syphilitic, cervical, hyperplastic (syphilitic).
Varicose veins.
Tumor:
Fibroma.
Glioma by extension from brain.

Extrameningeal:

Disease of vertebræ:
Tuberculosis.
Tumor—especially myeloma.
Metastatic.
Osteomyelitis with epidural abscess.
Charcot spine.
Fracture of vertebræ.
Dislocation of vertebræ.
Abscess—epidural—not from vertebra.
Aneurysm, eroding.

FOCAL CORD AFFECTIONS—CLINICAL RÉSUMÉ

Onset.	*Etiology.*	*Progress of Symptoms.*	*Pathologic Condition.*	*Aids in Diagnosis.*	*Treatment.*
Sudden.	Trauma.	Symptoms of focal affections complete, tending to improve.	1. Intramedullary hemorrhage. 2. Fracture of vertebra. 3. Dislocation (1 may occur alone. More often all three are present). 4. Fracture of a diseased vertebra.	History of accident in 1, 2, 3. *x*-Ray should differentiate fracture, dislocation, and disease.	Expectant at first. Later orthopedic, and at times operative.
Rapid.	Acute infections.	Symptoms of obscure cord affection progressing rapidly, assuming a focal character and frequently resulting in complete transverse myelitis.	1. Myelitis, usually toxic; disintegration of cord focally. 2. Epidural abscess.	Patient shows evidence of bodily infection and focus of which may or may not be evident. *x*-Ray negative as a rule. Spinal fluid in (1) apt to be negative; in (2) shows the complete compression syndrome. Both bacteria free.	1. Expectant. 2. Operative.
Slow.	Chronic infections. Tumor.	Symptoms of slowly increasing pressure on cord at a given level.	1. Chronic syphilitic meningitis or meningomyelitis. 2. Tuberculosis of vertebra. 3. Charcot spine. Gumma spine. 4. Tumor of vertebra (usually metastatic). 5. Tumor of meninges. 6. Intramedullary tumors.	1 and 2 show other evidence of syphilis of C. N. S. Blood and spinal fluid tests usually positive in (1); negative in (3). *x*-Ray should show characteristic picture of (2), (3), and (4).	1 and 3 antisyphilitic treatment if the tests are positive for active syphilis; 2 and 3 orthopedic; 4, symptomatic; 5 and 6, operative.
	(Vascular.)			All will usually show spinal fluid compression syndrome, for most part "incomplete," but some the "complete" syndrome.	

Of far more value to us as clinicians is the accompanying classification, which I have prepared in the briefest and most dogmatic form, omitting exceptions to the general rule and pathologic subheadings for the sake of clearness. With this table before you, it will be observed that most focal cord affections may be placed in three general groups, according to whether the onset be sudden, rapid, or slow. It is further noticeable that the agents at work in the first two groups are two—trauma and acute infection; if we exclude the traumatic cases with sudden cord lesions and the acute infections, cases with rapidly progressive lesions, we have already eliminated a very considerable number of causes of focal cord affections. We then turn to the third and by far the most heterogeneous group—lesions of slow onset and progress—due usually to chronic infections and to tumors.

Fig. 181.—Fracture-dislocation of dorsal spine with complete disintegration of cord at this level. (Case of Dr. E. W. Taylor.)

GROUP I.—LESIONS OF SUDDEN ONSET

Here are included the very considerable number of cases of "broken back" and "broken neck," ordinarily described in text-books under "Injuries to the Cord." The diagnosis is usually obvious. There has been an accident, perhaps a heavy weight has fallen on the spine, or the body has been suddenly bent into an awkward position, "something cracks," and the result is a complete paralysis below the point of fracture or dislocation. A not infrequent cause is a dive into shallow water with sudden wrenching of the neck.

Case I.—The accompanying photograph (Fig. 181) shows well a wedge-like protrusion of a dorsal vertebra, accompanied by fracture, which has completely severed the cord, although the dura is still intact; the accident was in a boy who was thrown over backward, striking the back of his head and neck. Needless to say there was immediate paralysis of legs and lower part of body with total loss of sensation and sphincter control. Bed-sores developed and death ensued after a few months.

Fig. 182.—Bilateral dislocation of seventh cervical vertebra on sixth cervical. From falling from wagon.

Case II.—Mr. A. M., fifty years of age, fell from a wagon and struck on the left side of his head. He was unable to move his legs and his arms were almost completely paralyzed; there was complete anesthesia extending to level of third intercostal space; above, zone of hyperesthesia. Deep reflexes absent. In this case (Fig. 182) *x*-ray shows a bilateral dislocation of the

seventh cervical vertebra on the sixth, with little evidence of fracture. Attempt at bloodless reduction was only partially successful and open reduction was resorted to, with good operative result (Fig. 183); the trauma to the cord had been so extensive, however, that little change resulted from the operation.

Hematomyelia, without fracture or dislocation or of insignificant extent, is of frequent occurrence. In such cases the clinical

Fig. 183.—Same case as Fig. 182. Open reduction and wiring. No improvement in spinal cord symptoms of complete transverse lesion.

picture soon after the accident may be that of transection of the cord, but with absorption of the hemorrhage and edema impulses may soon begin to pass along the cord, and the ultimate amount of destruction may not be great. As the hemorrhage tends to confine itself to the gray matter of the cord the long projection fibers are frequently spared in such cases, and the resultant paralysis tends to be referred to the cells of the segment or segments in

which the hemorrhage has occurred. Figure 184 represents a severe hematomyelia without vertebral fracture or dislocation. Such cases are to be treated expectantly.

At times we meet with patients who have an alternating paralysis following trauma. In one position the patient will be paralyzed, in another he can use his limbs; here we must admit a physiologic shutting off of nerve impulses from recurring transitory pressure. Fixation or operation are here imperative.

"Compression fracture" results from blows received and transmitted vertically rather than from the side or the back. In these the *x*-ray shows the bodies of the vertebræ fused and

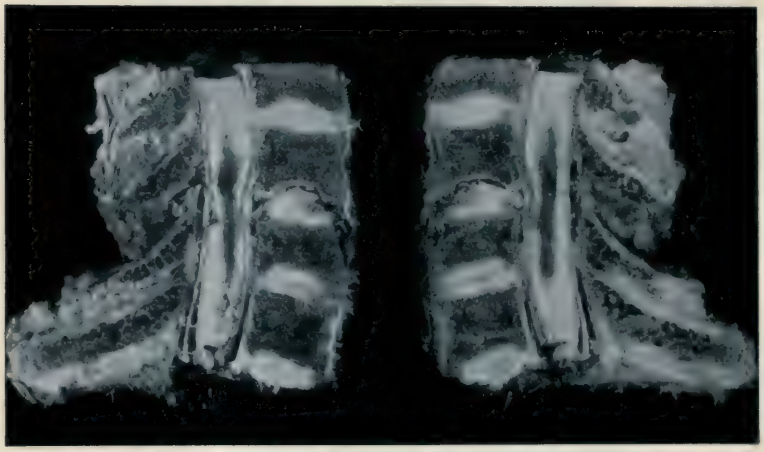

Fig. 184.—Hematomyelia from trauma. Little or no evidence of fracture.

laterally displaced, but the symptoms are rather of nerve-root origin, the cord usually escaping injury.

In this group we must also consider cord injuries received from fracture or dislocation of diseased vertebræ with sudden effects. As a rule, however, unless there is the additional element of trauma, the diseased vertebra exerts its influence by slow compression of the cord, and more properly should be classed in Group III. Nevertheless spontaneous fracture of a diseased vertebra may take place, with resultant sudden injury.

In this group, then, we include hemorrhage into cord, laceration of cord, and pressure upon cord as result of trauma. Unless

completely severed or severely damaged the tendency is to improvement. Treatment is, for the most part, of an orthopedic nature; rarely does open surgery do more than can be done with the properly applied brace. On this point, however, there is

Fig. 185.—Dislocation and fracture of cervical vertebra from trauma. In this case there was injury to motor and sensory nerve roots, but *no affection of the spinal cord*. The extent of trauma as indicated by *x*-ray is no criterion as to the extent of injury to the spinal cord.

difference of opinion, a number of writers on cord surgery in the present war advocating strongly more frequent laminectomy at the earliest possible moment in traumatic spinal cord conditions.

GROUP II.—LESIONS OF RAPID ONSET

Although "transverse myelitis" is the term colloquially used in describing the various conditions under consideration, it is rarely that a pathologic picture answering to this condition is seen. True, we not infrequently make such a diagnosis clinically; a patient with some infection, notably pneumonia, develops a rapidly progressive transverse lesion of the cord, and at death a disintegration of the cord substance is found. Organisms are not demonstrable, and the condition is put down as toxic in origin, although small vascular thrombi are said to play a part. Usually

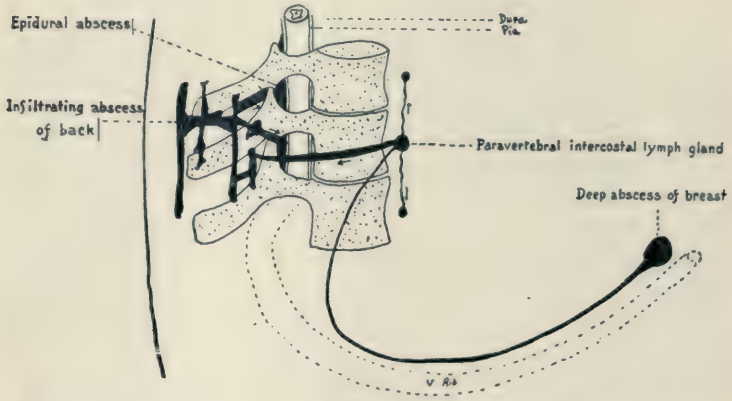

Fig. 186.—Diagram to show course of infection from deep breast abscess by intercostal lymphatic to lymph-node; thence by direct extension to back muscles and epidural space.

the process is severe, but improvement may occur to a considerable extent if the patient live. I have never seen this picture of toxic transverse myelitis from bodily infection, though I have several times made such a diagnosis in the living. Two cases, however, presented this pathologic condition in the medulla, in one case associated with a large chronic liver abscess.

The picture of toxic myelitis was produced in the case of a man presenting an epidural abscess which subjected the cord both to pressure and toxic influences. Although a rare condition, yet because of its importance from the therapeutic point of view and because the clinicopathologic data may here be traced

so clearly, it will be well to present the case in full, with abstract from a published article[1] (Fig. 186):

O. J., forty-three years, on August 20, 1915, while roofing a house, scratched his right breast on a nail; from this an abscess developed, and on September 3d broke, yielding subsequently to surgical treatment. About September 11th, however, the patient complained of "pleurisy pains" in left back and later also in left lower chest, which persisted, accompanied by a temperature of 102–104° F. On September 26th he could not pass urine for the first time, and complained of pains in legs as well as back. His back was rigid and tender over the seventh and eighth dorsal spines. The next day he had difficulty moving his legs, and by September 29th he was paraplegic, with urinary and fecal incontinence. Neurologic examination showed, besides the almost complete paralysis of legs, a mild bilateral sensory disturbance below umbilicus; knee-jerk present, ankle-jerk not obtained, plantars normal, abdominal and cremasteric reflexes absent. Head and arms not remarkable. Examination of the back showed some fulness only in dorsal region and crackling râles at bases of lungs. Lumbar puncture gave 4 c.c. only of clear yellow fluid, under no excess of pressure; the fluid clotting almost immediately. In twelve hours the fluid separated spontaneously from the clot and was found to give a negative Wassermann, a gold sol in the "meningitis" zone, great excess of proteins, and to be sterile on culture; the clot was macerated, and examined for cells, one only being found.

In seven days the patient died.

Abstract of Autopsy (five hours postmortem): Just to the right and below right nipple is an area, 10 cm. in diameter, of granulation tissue; from it no pus can be expressed, nor is there any in the surrounding tissue. The first incision into the back, however, yields a thick greenish pus; investigating deeper and more extensively shows that this pus has infiltrated the trapezius, latissimus dorsi, and erector spinæ groups of muscles. Dissecting to the spinal column, pus is seen to well up between the vertebræ, and when the laminæ and spines have been removed, a thick coating

[1] Ayer and Viets: Boston Med. and Surg. Jour., clxxv, p. 865, 1916.

of pus hides the dura from view for a distance of 10 cm., corresponding to the fifth, sixth, and seventh dorsal vertebræ. The pus is easily stripped from its position on dura and from the nerve-roots which it surrounds, leaving the former perfectly normal in appearance. The dura opened reveals a glistening inner surface and a cord of normal appearance, but the spinal fluid in the lumbar sac is of yellow color and, as analysis shows, is similar to that withdrawn previously. Even on section the cord presents everywhere normal appearance and markings.

Turning now to the pleural cavities: both contain a small amount of serofibrinous fluid and a few fibrinous adhesions, especially posteriorly on the right. On cutting through the pleura at this region pus exudes, and search shows that it comes from two sources, the erector spinæ muscles and necrotic paravertebral intercostal lymph-glands, the latter being affected more particularly in the neighborhood of the fifth dorsal vertebra.

Other postmortem findings are inconsequential. Cultures: pus from the back muscle; pericardial fluid and fluid from right pleural cavity—Staphylococcus albus in pure culture. Heart's blood, no growth.

Microscopic examination was carried out in routine manner on the tissues of the body, without striking addition to the gross findings. Microscopic examination of the spinal cord is, however, of considerable interest and importance, and is here given. First to be noted is that there is no distortion of the cord in the region of pressure and the size of the cord is not diminished; in fact, sections at one level suggest an actual, though slight, enlargement of the cord, fibers being separated more than normal, with presence of vacuoles, the cord at this point to the naked eye giving a moth-eaten appearance. While there is no certain destruction of nerve-fibers, such degeneration is suggested by the presence of a few phagocytic cells in the rarefied areas of the white matter (Fig. 187). Throughout the white also, but more particularly near the rim of the cord, a moderate increase in number and size of neuroglia cells is seen, some with faintly staining protoplasm; no evident increase of glia fibrils is to be seen. The gray matter pre-

sents normal configuration; the anterior horn cells are present in correct number, but many present the axonal reaction. Vessels appear normal and there is no evidence of dilatation or cellular infiltration of perivascular spaces. The pia is of particular interest because of its proximity to the abscess, which is separated from it only by dura. The pia shows a slight cellular infiltration, and on close examination the cells are found to be largely fibroblasts

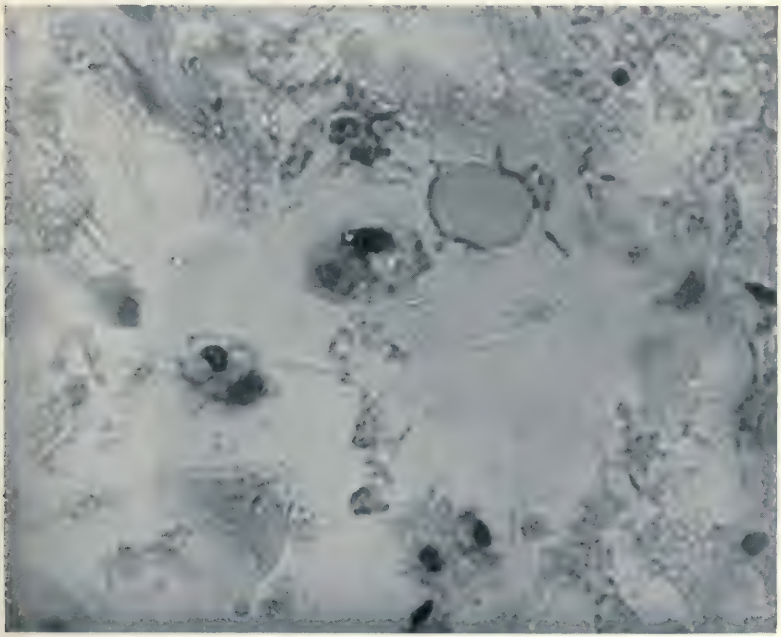

Fig. 187.—Photomicrograph of cord compressed by epidural abscess (Case III). Shows degeneration of nerve-fibers in white matter with phagocytosis—a condition of "compression-toxic-myelitis." The spinal fluid was free from bacteria.

with a few plasma cells and lymphocytes; no polynuclear leukocytes are seen in the pia. Nerve-roots, both dorsal and ventral, show perhaps a slight increase in fibroblasts, but no evidence of exudative cells.

It would take too long to go into the interesting possibilities of toxic degeneration of the cord from infections at a distance or by extension along nerve-roots. By far the most important contributions on this subject have come from Orr and

Rowes and their collaborators,[1] whose articles are of a most stimulating character.

GROUP III.—LESIONS OF SLOW ONSET

In dealing with the third group we find that we are concerned with an actually greater number of cases, of more various etiology, and also of more wide-spread manifestation—hence a more difficult problem. And yet in this group it is fully as important that an accurate diagnosis be made. One circumstance is to our advantage, we may safely take more time in studying a given case, and receive what benefit may be derived from continued observation.

Chronic infections—principally tuberculosis and syphilis—are responsible for a very considerable number of cases of focal cord lesions. These infections, however, do not act always in the same manner, either may act directly on the cord by destruction and replacement of medullary substance or by pressure from diseased vertebræ.

Syphilis.—The more common form of syphilitic transverse lesion is best described as meningomyelitis. Such a lesion occurs only in the course of a chronic spinal syphilitic meningitis. This form is rarer than formerly because it is a type of syphilis amenable to treatment. It should be readily recognized by other signs of syphilis of the nervous system and by the characteristic laboratory tests. "Charcot spine" and gumma of vertebræ are probably not so rare—at least the former—as is generally thought. One does not often find the diagnosis in card indices (only four times for the former in some twenty years at the Massachusetts General Hospital), but I can myself recall more than that number in the past six years.

Case IV.—Mr. L. B., a patient with typical dorsolumbar tabes, was treated by me medicinally with benefit. He, however, still suffered from the effects of marked cord degeneration. The next year I was asked to see him because of renewed pains.

[1] Orr and Rowes: Review of Neurology, p. 345, 1907. Jour. Mental Sci., lx, p. 184, 1914.

Orr and Rowes and Stephenson: Jour. Mental Sci., lxi, p. 411, 1913.

His condition had changed markedly; he now complained solely of severe pains about the lower abdomen and there was found well-marked anesthesia to touch up to this level; although knee-jerks remained absent, he now presented also double Babinski sign. On examining the back a slight kyphos in the dorsolumbar

Fig. 188.—Charcot spine occurring in a patient with marked degenerative tabes. Symptoms of incomplete transverse cord lesion and presenting the "incomplete compression fluid."

region was visible and *x*-ray showed vertebral calcareous deposits characteristic of the condition seen in Charcot joint (Fig. 188).

Unfortunately Charcot joints (of all kinds) in my experience occur in the late degenerative stage of tabes, frequently in cases stationary (*i. e.*, negative) from the laboratory point of view. Hence we could theoretically—and actually this is borne out by

experience—expect nothing from antisyphilitic treatment. We must here rely solely upon the application of a brace.

Tuberculosis is rarely the cause of a transverse lesion from involvement of the cord itself, although one case of solitary tuberculosis of the lumbar cord appears in my series. Tubercular meningitis runs too rapid a course to become focal in character,

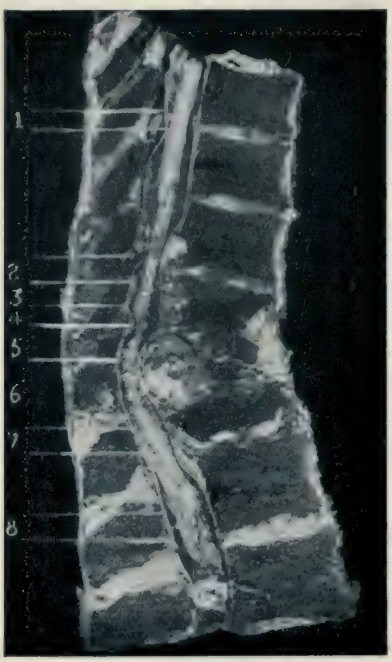

Fig. 189.—Hemisection of spine from seventh thoracic to second lumbar vertebra inclusive, showing tuberculous process especially developed at the eleventh thoracic vertebra. (Case of E. W. Taylor.)

and consequently its effects are too wide-spread to give transverse lesions. Pott's disease, however, is one of the commoner causes of pressure upon the spinal cord, but only when the tubercular focus bursts its vertebral borders is it in position to damage the cord (Figs. 189 and 190).

In Pott's disease the *x*-ray should be of great assistance, but occasionally, due perhaps to an inconveniently situated vertebra,

this fails, and perhaps even an operation may be performed on such a case for supposed cord tumor.

CASE V.—That operation is not a fatal mistake is shown by the case of a young woman in whom were signs of moderate pressure in the cervical region, spastic-ataxic gait, with level of cuta-

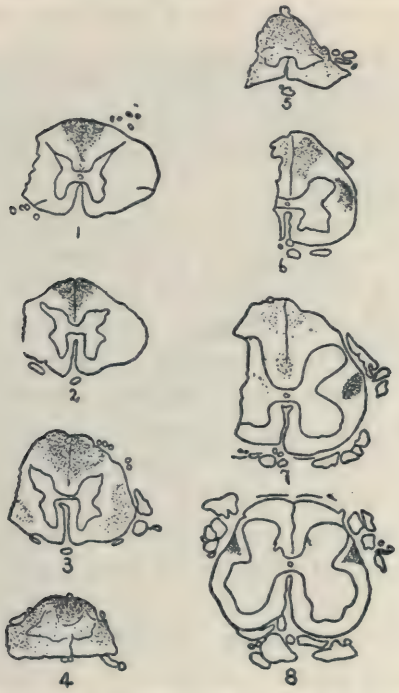

Fig. 190.—Cross-sections, showing areas of degeneration at the eight levels studied. (See Fig. 189.) Edinger drawing apparatus; accurate tracings. The defect in the sections, especially in 1, 2, 6, 7, is due to the fact that a preliminary hemisection of the spine with the cord *in situ* was made. The deformity of the cord, due to actual pressure, is shown in 4 and particularly in 5, being in sharp contrast to the well-preserved general contour of the other levels. (Case of E. W. Taylor.)

neous anesthesia, together with the incomplete spinal fluid syndrome. Operation revealed a bulging of the anterior dural wall and the probe unexpectedly revealed pus in the vertebral protrusion. Contrary to our fears, in this case the patient did not develop tubercular meningitis, although the dura had been

opened. Recently, three years after the operation, I have seen her, walking naturally and quite well.

Tumors exert pressure upon the spinal cord from without and from within, the symptomatology varying considerably with the different types.

Tumors of the vertebræ with pressure upon cord after erosion are usually metastatic, the breast furnishing one of the chief original foci. Pain from involvement of sensory roots is apt to precede cord pressure in such cases, at which time the diagnosis is not easy; when, however, the tumor has reached sufficient size to cause pressure the diagnosis is usually clear enough from examination and *x*-ray.

Tumors of the meninges and of the spinal cord itself, on the other hand, are often difficult of detection at any stage—to differentiate type and locus of such a tumor early is one of the fascinating problems of neurology. In the early detection of the presence of tumor, broadly speaking, as differentiated from some other disease of the cord, we are placing more and more reliance on the spinal fluid findings. Tumors early give the incomplete syndrome in most cases. Given, then, a case of probable pressure upon the cord, we search carefully for symptoms and signs for localization of level, waiting, if necessary, weeks or months for their development. Operation is then advised as the sole effective means of cure.

The following case, given in brief, represents a happy outcome of such a case:

Case VI.—Miss N. L. in January, 1914, presented a partial Brown-Sequard syndrome of eight weeks' duration, and a probable diagnosis of syringomyelia was made. Spinal fluid clear, colorless, proteins much increased, cells 8, Wassermann negative. Gold sol, 0, 0, 1–2, 2, 2, 3, 2, 2, 1, 0. December, 1914: Increase of all cord symptoms, approaching "transverse myelitis." *x*-Ray of spine negative. Spinal fluid substantially the same. August, 1915: Level of transverse cord affection established at D. 4. Is now unable to walk. Double clonus and Babinski. Spinal fluid still shows incomplete pressure syndrome. Operation. Extradural endothelioma, size of Eng-

lish walnut, pressing on D. 6, and attached to dura; tumor removed entire. Complete symptomatic recovery.

More often, with similar symptoms, an irremovable tumor is found, as, for example, a glioma growing in the cord substance (Fig. 191), but with earlier and more accurate diagnosis even some of these intramedullary tumors may be operated upon with benefit.

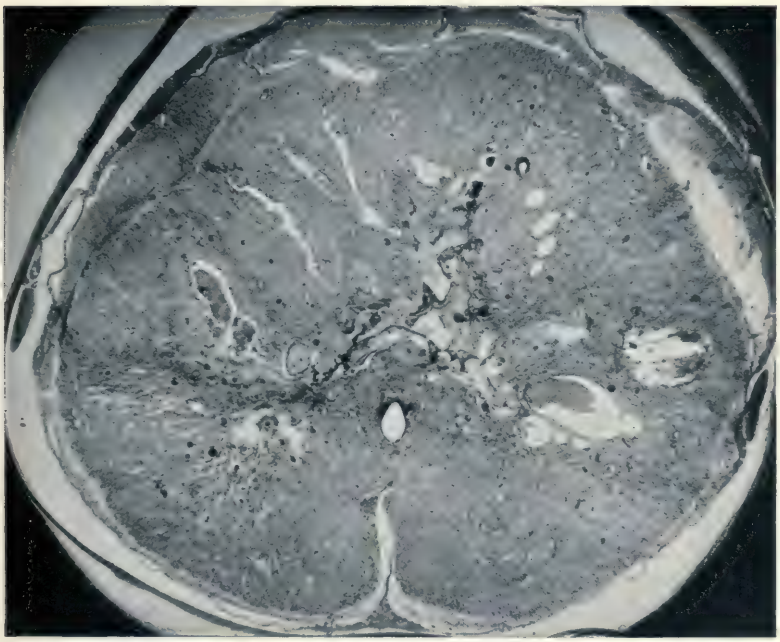

Fig. 191.—Gliosis spinalis. Almost complete replacement of cord substance by gliosis, an incident in this case of the course of syringomyelia.

In the foregoing we have rapidly passed over a considerable array of pathologic entities, the one point in common among them being their capacity for producing focal affections of the spinal cord. It is most important for the proper treatment of patients suffering from such a highly destructive condition that an accurate diagnosis be made early and as accurately as possible. The separation into groups, as above given, with recognition of the chief types of disorder appertaining to these groups, in my opinion,

clears the mind for a differential diagnosis which, while frequently not certain, serves the purpose for action or inaction in a given case and a rational treatment in all.

Once more it is well to restate the importance of the best possible *x*-ray and most careful spinal fluid examinations as indispensable aids in establishing an early and accurate diagnosis of compression of the spinal cord.

CLINIC OF DR. RICHARD M. SMITH

MASSACHUSETTS GENERAL HOSPITAL

PYELITIS OF INFANCY

Definition; Occurrence; Symptoms; Signs; Pathology; Course of the Disease; Complication of Other Diseases; Mode of Infection; Illustrative Cases; Treatment.

BY the term "pyelitis" is meant an inflammatory condition of the pelvis of the kidney associated with bacteria and pus in the urine. It is sometimes called cystitis or pyelonephritis, and is to be differentiated from so-called acute hemorrhagic infection of the kidney.

Pyelitis is a very frequent disease, constituting about 1 per cent. of all cases coming to the physician dealing with children. It occurs at any age. The youngest case which I have seen was in a boy two days old; another was in a boy five days old. It is stated that the disease is much more frequent in girls than in boys. This is true after the sixth month, but before that time the difference in sex incidence is not very great. Beyond the sixth month there are about three times as many cases in girls as in boys.

The disease begins frequently with symptoms of the digestive tract—vomiting and diarrhea—and sometimes these persist for a considerable number of days and are severe enough to mask the real cause of the trouble. Urinary symptoms are usually very slight or absent. If present, they consist of frequency of micturition and sometimes of pain. There is often evidence of general discomfort quite possibly associated with abdominal pain. It is shown by irritability, sleeplessness, and refusal of food. Chills sometimes occur, and if they occur during the first year are practically pathognomonic of this disease. Chills are unusual in boys, but quite common in girls.

Physical examination rarely reveals any specific signs of this disease. Early in the disease temperature is usually present, it may be high and may continue for a variable length of time; from a few days to weeks. Pallor is usually present and may be of an extreme degree. There is also frequently general tenderness, greatest in the lower back, which may be confused with spinal disease. Sometimes the spleen is palpable. The diapers and clothes are often stained yellow by the pus in the urine, or brownish yellow if there is a good deal of blood. This staining, however, is not a constant occurrence, but is helpful when present.

The only sure sign of the disease is the finding of evidence of infection in the urine. It is advisable to examine more than one specimen of urine, as it not infrequently happens that a single specimen may be normal and a second specimen will reveal the disease. Albumin may or may not be present; its absence does not rule out pyelitis. The examination of the sediment is of primary importance. Usually an increased number of leukocytes will be found. More than three pus cells in the ordinary high dry microscopic field in girls and more than two pus cells in boys in the presence of symptoms described above warrant the diagnosis of pyelitis. Sometimes no cells or no increase of cells are found, but many organisms, usually bacilli, are present. If large numbers of motile bacilli occur in a fresh specimen, *i. e.*, one recently passed, or in a catheter specimen, the diagnosis of pyelitis is justifiable. When a secondary infection of the kidney occurs casts appear in the urine. Occasionally a hemorrhagic type of the disease is present in which there is a large amount of blood. This type is frequently difficult to differentiate from acute nephritis. The presence of many organisms and more leukocytes than would be accounted for by the blood favor pyelitis. Sometimes only the course of the disease can determine the diagnosis.

The failure to make a diagnosis of pyelitis is most often dependent on a failure to make a careful examination of the urine, probably because of the absence of urinary symptoms.

Pyelitis occurs not only as an independent condition but also

as a complication of other diseases, appearing in the height of the disease or subsequent to it. The examination of the urine often will explain a continued elevated temperature or a fresh rise in temperature during the course of the disease which otherwise was progressing satisfactorily. All children coming to the physician should have their urine examined, especially the sediment, in order that pyelitis may be either diagnosed or excluded as a possible cause of symptoms.

The following cases illustrate some of the many manifestations of the disease which have occurred in my own practice recently:

R. A. Seen when forty hours old. Baby was perfectly well until this morning, when he seemed to have some abdominal pain. The nurse took the temperature and found it to be 103° F. Physical examination was entirely negative except that the baby was slightly jaundiced. Movements consisted of meconium. No cause for temperature found. Cleaned out with castor oil. Temperature normal the next day, but rose again in two days, then came down to normal. Progressed fairly well for a month, then had a temperature of 102.8° F. again with a negative physical examination. A specimen of urine showed pus in considerable amounts. This was cured at the end of ten days by the administration of urotropin.

G. P. Age fourteen months. Negative previous history. Had no particular difficulty in feeding and had progressed satisfactorily. Without previous symptoms began to be irritable, fussy, and had a temperature of 103° F. A specimen of urine obtained was negative except for the presence of numerous motile bacilli. The temperature continued elevated. A second specimen of urine showed again many bacilli and an occasional leukocyte. The temperature remained elevated, sometimes going as high as 105° F., down to 102° F. for two weeks. The urine during this time showed no increase in cells, but showed repeatedly a marked bacilluria. At the end of two weeks the temperature dropped to normal and the urine was typical of pyelitis, with a large amount of pus. This patient was given urotropin together with the usual general and hygienic treatment, and

after several weeks the urine cleared and has remained so to date.

E. B. Age three years. Previous history unimportant. For about ten weeks she has been a little pale and somewhat constipated. Breath not good, A diagnosis of indigestion had been made and the fat reduced in the diet and iron given. She was a little better at first, but has continued to be pale and have a poor appetite. Never had any fever. Has lost 4 pounds. Physical examination negative except that she was a little pale. Routine examination of the urine showed four to six leukocytes in the ordinary high dry field and many motile bacilli. Was put on a full diet with 20 grains of urotropin every twenty-four hours, force fluids, and free evacuation of the bowels. Ten days later the urine contained a small amount of blood, apparently from the urotropin. The blood, however, disappeared with the omission of the drug. One month from the time first seen the urine was entirely normal.

M. T. Age seven years. Had been in excellent condition. Two days ago went to a children's party and has not felt well since. Given castor oil last night, which she vomited, and an enema this morning. Result contained a good deal of mucus. Temperature today 102° F. Physical examination entirely negative except for little superficial tenderness in the left side of the abdomen deep down. The urine showed pus in the sediment, otherwise negative. The temperature was normal in four days. The sediment was clear in one month. Was given forced fluids, rest in bed during the acute stage of the disease, and potassium citrate to make the urine strongly alkaline.

L. J. Age three years. Past history unimportant except that it was a premature baby. For the last six months every three weeks has had recurrent attacks of fever accompanied by vomiting, loss of appetite, and irritability. Has always been more or less constipated, and this condition is worse during the attacks. Recently the attacks have been more frequent, occurring every ten days. The urine had previously contained albumin and the protein had been cut down in the diet on that account. Physical examination was negative except that she looked pale.

Nothing abnormal in the abdomen discovered. Routine examination of the urine showed a few cells and many motile bacilli. Was put on a full diet and routine treatment of pyelitis with urotropin. Subsequent examinations of the urine showed frequently large amounts of pus and always many motile bacilli. In one month the sediment was normal. The "attacks of indigestion" have entirely disappeared.

E. A. Age eight years. Always been a well and strong child. Ten days ago began to have frequent micturition, and at this time the urine was acid. Sediment not examined. Given something to make the urine alkaline and nothing further thought about this condition. Six days ago had a temperature of 103° F. and complained of a good deal of pain low down in the abdomen. The next day the temperature came down, and she seemed better. The day after she had a good deal of general tenderness everywhere, and was discovered to have a slight vaginal discharge. The next day she seemed better in the morning, but in the afternoon she complained of pain in the abdomen. Question of an appendix. Blood count 20,000. Urine at this time contained a good deal of pus. The next morning the tenderness was on the right side of the abdomen. Temperature 104° F. Had a slight chill. When seen was lying comfortably in bed. Complained of pain in upper part of the abdomen. Examination outside of the abdomen was negative. Abdomen was held rigidly without any tenderness over the appendix. Nothing definite could be made out anywhere. The urine showed a large amount of pus and an occasional red cell and a few bacteria. The smear from vagina was negative for gonococci. Large doses of urotropin, with forced fluids, rest in bed, light diet, and open bowels prescribed. A little later a good deal of blood appeared in the urine. Given potassium citrate for a few days, then returned to the urotropin. After several weeks the child recovered and has had no subsequent attacks.

R. H. Age fifteen months. Previous history negative except that at eleven months she had a convulsion. For several weeks ran a high temperature and seemed very nervous, from which she recovered. Did well for three weeks, then she had

another convulsion. This was followed by German measles one week ago. Has entirely recovered from that. Has alwayd had a tendency to constipation. A specimen of urine obtained today showed a considerable amount of pus. Physical examination entirely negative. Temperature 100½° F. Given urotropin, forced fluids, light diet, open bowels, and general hygiene. After four days the urine was clear and remained so for two weeks, when she had another rise in temperature, with the reappearance of pus in the urine.

M. P. Age fifteen months. Previous history unimportant except is convalescing from whooping-cough. No digestive disturbances except tendency to constipation. Four days ago began to have a temperature and the movements were bad. Given castor oil and enemas. Did not vomit. Movements green and slimy. During the next two days vomited several times, and the movements continued to be bad. The temperature was elevated, grew very pale, and abdomen became distended. Seemed quite sick. When seen at this time the physical examination was negative. Urine showed many pus cells and many motile bacilli. Given urotropin, forced fluids, rest in bed, free catharsis, and in seventeen days from the first rise in temperature the urine was practically clear. Subsequent examination showed an occasional pus cell, but there was no return of symptoms. Further examination of the urine revealed a clear sediment and has remained so.

M. P. Age three and a half years. Has always been well. No digestive trouble. No fever of any sort. Five weeks ago the child had a convulsion in the morning, lasting four or five minutes. Had another one that day, another at night, and one in the evening. The next day seen by a physician in London, where they were at the time, who could find nothing on physical examination to account for the trouble. Was put on a limited diet, but a few days later had another attack which was slighter. Had no return of the trouble until seventeen days ago, when she had another slight convulsion which was rather different in character. No rigidity, no cyanosis, but a little twitching, lasting a few minutes. Came home three days ago. Stood the jour-

ney very well. Yesterday morning had a slight convulsion with almost no loss of consciousness. Since the onset of the first convulsion quite frequently, as often as once or twice a day, she has had times when she would draw back her head or drop an article if she had it in her hand. No real loss of consciousness. No staring, and not really typical of petit mal. No loss of sphincter control. She has had no other symptoms than those described above. Has had no headaches. No vomiting and no digestive symptoms. Seems in perfect health. Physical examination at this time was entirely negative. Routine examination of the urine showed a slight increase of cells and nothing else. Was put on a careful diet, given general directions for hygiene and care. The attacks continued without interruption. Frequent examinations failed to reveal anything further. Frequent examinations of the urine, however, showed an increasing number of pus cells. She was given potassium citrate and after about a month the urine was entirely clear. With the disappearance of pus from the urine, the attacks described above entirely ceased. There were two or three relapses of the attacks always associated with relapses of the pyelitis. For the last year there has been no pus in the urine and has had no further attacks.

B. D. Age eleven months. Well up to three weeks ago, when she had a little time of crying, fussy, with slight elevation of temperature. She apparently entirely recovered from this. Last three or four days has been fussy and has vomited three times. Vomiting has now ceased. The temperature is still elevated. Given water, barley-water, and broths. Stools have been normal. Objects to being handled. Has lost a great deal of weight. Temperature is 103° F. Physical examination is negative except that she looks pale and cries if disturbed The urine showed pus. Given forced fluids, open bowels, and urotropin.

M. P. Age eleven months. Previous history unimportant. Always been well. For four or five days has been rather fussy. Little temperature. Refusing some of food. Temperature is 104° F. Physical examination entirely negative except that she is pale. Previously has had excellent color. Examination of the

urine showed a moderate amount of pus. Was put on a light diet, forced fluids, open bowels, with potassium citrate. At the end of two months the urine was entirely normal and has remained so since.

Pathologically, pyelitis shows only an inflammatory reaction at the pelvis of the kidney, consisting of an increased number of cells and the presence of bacteria. The substance of the kidney is normal unless it becomes secondarily infected from the pelvis of the kidney. When such a secondary infection occurs there may be a very marked destruction of the kidney resulting in the prolonged and severe cases in practically entire destruction of the organ. The kidney function is decreased during the acute and early stage of the disease, but subsequently, unless there is a secondary infection of the kidney itself with destruction, the function is normal.

Cultures from the urine show the presence of virulent organisms. In about 75 per cent. of the cases colon bacilli are found. In the remainder a variety of organisms—streptococci, staphylococci, and others—are found.

The course of the disease is variable. The children with acute and severe symptoms in general do better than those with a less virulent onset. The acute stage usually lasts only a few days, or rarely weeks, during which time the temperature is elevated. After the fall in temperature the urine still shows the presence of bacilli or cells. The tendency of the disease is to become chronic. Relapses occur without apparent cause, but are frequently associated with acute infections even a considerable time after the attack. Considering these facts, it is difficult to say when a given patient is cured. When bacilli are present in the urine in considerable numbers, as can be easily determined from a stained centrifuged specimen, and when cells are present in the sediment, even though the patient is without symptoms, the disease cannot be called cured. If, however, the urine is sterile and there are no symptoms the case is certainly cured. The patient may be cured so far as the need of treatment is concerned, even though a catheter specimen of the urine shows the presence of organisms.

Pyelitis without complications is almost never fatal, but in protracted cases intercurrent infections, especially pneumonia, are common.

There has been much discussion as to the mode of infection of pyelitis, *i. e.*, how the organisms get into the pelvis of the kidney. Three main theories have been advanced: first, ascending; second, direct transfer from the colon; third, blood.

In the ascending infection it is assumed that the organisms enter the urethra, then the bladder, pass along the ureter into the pelvis of the kidney. This theory is advanced because of the greater number of cases in girls, and the fact, with the short urethra and its easy contamination, would seem to suggest this mode of infection. There has been no conclusive experimental work to support this theory, and a considerable amount of work has been done to prove the impossibility of infection in this manner. It seems to me that although theoretically it is a possible mode of infection, practically it is not to be considered.

Direct transfer of bacteria from the colon to the kidney via the lymphatics is possible. It has been shown by anatomic studies that there is a direct lymphatic connection between the colon and the kidney. This connection is more intimate on the right side, and pyelitis when unilateral is more common on the right side. So far as this evidence goes it indicates that this may be a possible means of infection.

Recent work has tended to establish the blood as the usual means of infection. The probable course is somewhat as follows: The organisms enter the blood from the intestinal tract or other parts of the body. Entering the blood directly or through the intermediary of the lymphatics, they pass with the blood into the kidney, through the glomeruli, down the tubules, and out at the pelvis. During the passage through the kidney they may or may not cause an infection. What happens depends upon the virulence of the bacteria and upon the general resistance of the patient and the local resistance of the kidney. Colon bacilli have a low pathogenicity, therefore rarely cause infection in the kidney. In being excreted at the pelvis an inflammatory process occurs, causing the disease pyelitis. There may be an

infection of the kidney by extension inward from the pelvis via the lymphatics, but it is not directly associated with the primary condition. A large amount of experimental evidence has been collected to substantiate this mode of infection, and all the various steps in the process have been shown possible of occurrence.

The discussion of the mode of infection has more than an academic interest, because if this third method, namely, via the blood, is the true method, as I believe it is, it indicates that we must search out the portal of entry of the bacteria if we are to treat the disease intelligently or be successful in preventing its occurrence.

The intestinal tract is undoubtedly the source of infection in the majority of instances. The close connection between the intestinal tract and the disease is shown by the great frequency of pyelitis as a complication of the acute intestinal infections in infants. The mucous membranes about the vagina and penis where colon bacilli are present in large numbers furnish also a possible source of infection in many cases. This is particularly true where there is local irritation causing excoriation. Suppuration or infection anywhere in the body may furnish the portal of entry for bacteria into the blood-stream. The following cases suggest these various sources:

J. M. Age five days. Normal at birth and normal delivery. Two days ago had a temperature of 104° F., down to 101½° F. yesterday afternoon, but is 104° F. today. Has lost weight steadily since birth, although mother seems to have plenty of milk. Took food well until today, when he has not taken it so well. Given a teaspoonful of castor oil yesterday. When seen was jaundiced. Did not look sick. Physical examination was negative except for five or six pustules on the right side of neck. The skin condition was given appropriate treatment. A specimen of urine obtained showed a large number of pus cells, many of them embedded in mucus, and many cocci. Was given urotropin, force fluids, and the urine entirely cleared. It is possible that the impetigo was the source of infection in this case.

C. H. Age fourteen months. Previous history unimportant.

Has done very well. Never been able to take orange-juice because of burning movements. Was given orange-juice day before yesterday, and yesterday had two or three loose stools which caused marked excoriation of the buttocks. This morning had a temperature of 102° F. and is very fussy. Physical examination except for the local condition of the buttocks was entirely negative. The urine showed a large amount of pus and many motile bacilli. Was given urotropin and the temperature came down to normal in two days. At the end of ten days the urine was normal and has always remained so. It is quite possible that the excoriation around the buttocks furnished the portal of entry for the bacteria in this case.

E. O. Age two weeks. Normal birth. Artificially fed because the mother died at birth. Was fairly well nourished. In a good condition except for a marked excoriation around the vulva, inner side of thighs, and back. Routine examination of the urine showed many pus cells and bacilli. Was given urotropin, forced fluids, and light diet. The urine cleared rapidly.

F. L. Age two years. Previous history unimportant. Has always done perfectly well. Yesterday began to have a slight cold. Temperature 102° F. Glands in both sides of neck swollen. Physical examination except for a reddened throat and the enlarged glands in neck was negative. This case was one of a septic sore throat epidemic due to milk. The throat pursued its usual course. Routine examination of the urine showed five days after the onset a typical pyelitis. The throat and the urinary condition progressed favorably and was entirely cured at the end of three weeks.

The **treatment** of pyelitis consists in rest in bed during the febrile stage, in general hygiene, and in the use of certain drugs. It is of the greatest value to pay attention to the condition of the bowels. The disease is frequently associated with chronic constipation. Attacks may recur or grow worse when constipation is present. Therefore, as a means of prevention and of treatment, a free evacuation of the bowels should be accomplished each day.

Acute general infections undoubtedly lower the resistance of the individual and thus give the colon bacilli or other bacteria

which may be passing through the kidney a chance to set up an infection. The local infections, such as nasopharyngitis, carious teeth, furuncles, etc., furnish possible sources of disease. Every means should be employed to increase general resistance and to remove possible portals of entry for bacteria. Fluid should be taken in more than the usual amount, not less than 3 pints in the twenty-four hours, to prevent the concentration of bacteria.

In the acute or early stage of the disease hexamethylenamin or urotropin is the drug to use. This should be given in sufficient amounts to produce results, even though it causes vesicle irritation or hematuria. No permanent damage is done and it is better to push the drug to a point where results are obtained than to give small doses for fear of producing hematuria. The urine should be tested to be sure that formalin is present. It is to be remembered that formalin is liberated only in acid urine, so that unless the urine is acid, either acid sodium phosphate or sodium benzoate should be given. The number of grains of urotropin to be given in each twenty-four hours depends upon the individual case, but infants under one year can be started at 20 grains in the twenty-four hours and the dose increased from this point if necessary. When urotropin is not effectual, potassium citrate or sodium bicarbonate may be given to render the urine alkaline.

Sometimes the rapid varying of the reaction of the urine from acid to alkaline will make the growth of the colon bacilli in the urine less easy, and thereby influence favorably the course of the disease.

Vaccines have been tried in this condition, but I have not been convinced that they are of any value. If used, they should be used in large doses, and discontinued if no good results are obtained after three or four doses.

In older children local application of silver salts to the pelvis of the kidney may be effectual in very stubborn cases. This method of treatment is inapplicable in children under six years of age.

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THE CAUSE AND TREATMENT OF BRONCHIAL ASTHMA

A Discussion of the Facts which may be Elicited from the Patient by a Careful History; the Relationship between Anaphylaxis or Protein Sensitization and Bronchial Asthma; a Test for and the Discussion of Protein Sensitization in Asthmatics; a Clinical Classification of Bronchial Asthma; the Presentation of Cases Illustrating the Different Types and Causes of Bronchial Asthma According to this Classification and a Discussion of the Treatment of Bronchial Asthma.

SINCE the present methods of determining the cause and treatment of patients with bronchial asthma are of recent origin and are not generally known it seems advisable before the presentation of cases to show how a case of bronchial asthma is analyzed; in other words, how one determines the cause of bronchial asthma in a patient.

A very careful history relative to the disease in each patient is essential; the following facts, although not infallible, are of great help and may be elicited from the patient. The age of onset of asthma is very important. The onset of asthma during the first year of infancy should lead one to suspect milk as the cause; onset during the second year of age is due usually to eggs, cereals, and wheat flour, frequently to bacteria, and rarely to other substances. The presence of eczema with asthma is very strong evidence that some food is causing both eczema and asthma at this early age. Throughout childhood between the ages of two and twelve the frequency of foods as a cause of asthma gradually decreases with age and the frequency of bacteria as

a cause gradually increases. During this period of years the acute infections of childhood play a great part in the cause of asthma. Chiefly among these infections are whooping-cough, measles, and severe prolonged colds, all of which usually have bronchitis as a complication or sequel, and the bronchitis predisposes to asthma; naturally, bacteria are the true cause of asthma in such conditions. During childhood two additional causes of asthma present themselves: exposure to animal emanations and to plant pollens. Between the ages of twelve and forty foods are rarely, and bacteria are usually, the cause of asthma. During this period of life the onset of asthma is usually associated either with repeated attacks or with one prolonged attack of bronchitis, with frequent head and chest colds, and occasionally with other acute infections. Plants and animals are also frequently the cause of asthma at this time. Of the animals, the horse is the chief cause and the cat is a frequent cause; other animals play a minor rôle. Of the plants, it is chiefly those which pollinate during the summer months, therefore the asthma caused by plants is a summer type. The pollen of red top and timothy is usually the cause of that type of asthma which patients have only during June and July, and the pollen of ragweed and golden-rod is the chief cause of that type of asthma which patients have only from the middle of August to the first frost. The pollen of daisy may link together these two types of summer asthma, so that asthma may be continuous from early in June to the first of October, in which case the pollen of these five plants is the cause. Occasionally this summer type of asthma is so violent that there is a resultant bronchitis and consequently bacteria may prolong a true pollen asthma for months or even throughout the year. The onset of asthma after the age of forty is practically always caused by bacteria, and the asthma usually manifests itself at first as a bronchitis which gradually increases in severity. Naturally after the age of forty disease of the heart and kidneys may play an important rôle in the cause of asthma; physical examination, however, will verify or eliminate these and other organic causes. With the exception of bakers (inhalation of wheat and other cereal flours) and care-

takers of horses, occupation, as a rule, has little bearing on the direct cause of asthma. Although heredity may predispose to asthma, it has no bearing on the causative agent. Asthma recognizes the four seasons of the year. A small group of patients have asthma only during the winter months when the air is clear and cold; a large group of patients have asthma only during the spring (March and April) and fall (October and November), months when the weather is very changeable and unsettled. These seasonal types of asthma practically always are associated with bronchial colds and bronchitis, and obviously bacteria are the primary cause. In a few instances the summer type of asthma is caused by bacteria; bronchitis is an important factor.

Having outlined the various causes of asthma, we may now consider the sources of entrance into the body. There are three sources: inhalation, ingestion, and infection. Inhalation takes place through the respiratory tract and chiefly concerns the pollen of plants, the emanations, hair and skin excoriations of animals, and in the case of bakers and housewives the inhalation of the flour of the cereal grains. Ingestion has to do with the eating of foods, and we know that, for some not well-understood reasons, foods after entering the gastro-intestinal tract do cause asthma. By infection we mean the presence of pathogenic bacteria in any part of the body, but such foci are usually present in the teeth, tonsils, nose, throat, and lungs.

We know that foods, bacteria, plant pollen, and the excoriations of animals are very complex substances, and that many different elements make up their complex. Therefore it must be determined what part of these substances enter into the cause of asthma. Fortunately, this problem has finally been settled as a result of prolonged investigation, and we now know that it is the protein in these substances that causes asthma. (In the case of bacteria, however, besides the protein element we also have the infectious element, which will be considered later on.) We will now briefly outline the development of investigations which associates proteins with the cause of bronchial asthma; these showed that patients may be sensitized to proteins, that proteins are responsible for anaphylactic shock, and that ana-

phylactic shock in animals simulates an attack of bronchial asthma in the human. The earliest observation having direct bearing on protein anaphylaxis is found in the writings of Magendie in 1839. He describes the sudden death of dogs which had been repeatedly injected with egg-albumen. Richet in 1902 made a systematic study of this problem and found that the first dose of protein was followed by a condition of markedly greater susceptibility to the protein. He called this phenomenon "anaphylaxis" to express its antithesis to prophylaxis or protective effects. As a result of the work of many other investigators from this time on we now know that when a specific antigen (a protein in the case of asthma and anaphylaxis) meets its antibody the reaction between them gives rise to a toxic product, and this causes the characteristic symptoms known as anaphylactic shock. In 1910 Meltzer pointed out that in both bronchial asthma and anaphylaxis the symptoms consist in a tonic stenosis of the small bronchioles, and that both conditions are favorably affected by the administration of atropin.

From the work of many investigators we now know a considerable amount about anaphylactic shock in animals. In our study of bronchial asthma we have been able to show to a certain extent that a similar type of anaphylactic shock plays a rôle in asthma in man. If a bronchial asthmatic who is sensitive to some protein be injected subcutaneously with a small amount of this protein, he will have shortly an attack of bronchial asthma. He has difficulty in expiring, but at first no difficulty in inspiring. Later, as the lungs become overdistended, there is difficulty also in inspiration. If the patient is examined with the fluoroscope at the time he is struggling for breath, we find that the lungs do not move and that the diaphragm is stationary in a depressed position. Immediately following an injection of adrenalin chlorid, however, the lungs are seen to expand, the diaphragm moves up and down with respiration, and the patient's dyspnea abates. Furthermore, an analysis of the patient's alveolar air during the paroxysm of difficult breathing shows that the alveolar air has a low carbon dioxid content, although the blood at the same time shows a normal carbon dioxid content. Following

the injection of epinephrin chlorid, which relieves the difficult breathing, the carbon dioxid content of the alveolar air gradually returns to the level of that in the blood. Thus attacks of bronchial asthma and anaphylactic shock are similar, in that both may be caused by proteins, and the symptoms are similar, in that there is labored respiration. Pathologically, the two conditions are alike, in that there is distention of the lungs, and furthermore in animals there is a stenosis of the bronchioles, and in the human body there is evidence of this from the carbon dioxid content of the alveolar air. And, lastly, both conditions are relieved by injections of epinephrin chlorid.

Having thus shown that it is the protein element in substances which may cause asthma we must next consider how it is possible to ascertain whether or not some particular protein may really be the cause of asthma. There are two tests which may be applied to the patient in order to determine protein sensitization. One of these is an intradermal test, which we will not describe since we consider it to be impracticable and erratic. The other test is known as the skin or cutaneous test, and since we have found this test to be practicable and reliable a description of it will follow:

A number of small cuts, each about $\frac{1}{8}$ inch long, are made on the flexor surfaces of the forearm. These cuts are made with a sharp scalpel, but are not deep enough to draw blood, although they do penetrate the skin. On each cut is placed a protein and to it is added a drop of tenth-normal sodium hydroxid solution to dissolve the protein and to permit of its rapid absorption. At the end of a half-hour the proteins are washed off and the reactions are noted, always comparing the inoculated cuts with normal controls on which no protein was placed. A positive reaction consists of a raised white elevation or urticarial wheal surrounding the cut. The smallest reaction that we call positive must measure 0.5 cm. in diameter. All larger reactions are noted by a series of plus marks, and any smaller reaction is called doubtful. As evidence that the skin test is satisfactory and conservative we have found by treatment with subcutaneous injections of proteins that we cannot inject a patient with a stronger solu-

tion of a protein than that which gave a positive reaction without producing an attack of asthma.

A few words seem necessary in regard to multiple sensitization or sensitization to two or more unrelated proteins. We find that the same patient may be sensitive to, and his asthma may be caused by, any combination of the proteins derived from plant, animal, food, or bacterial sources. We have found that most patients who are very sensitive to the proteins in horse dandruff are somewhat sensitive to the proteins in cat and dog hair. Only 20 per cent. of those patients that are sensitive to horse dandruff are also sensitive to horse-serum protein, so that a very small percentage of asthmatics are sensitive to horse-serum and the danger of injecting an asthmatic with moderate amounts of horse-serum, such as antitoxin, is confined to only a rare case. Horse asthmatics should not be given large amounts of horse-serum intravenously without previously testing the patient with horse-serum and horse dandruff; this naturally applies at the present time to antipneumococcus serum therapy. If the asthmatic is sensitive to horse dandruff proteins and not to horse-serum, he may be injected slowly with as much as 60 c.c. of horse-serum before signs of an asthmatic attack develop, and if the injection is stopped at this time no serious results follow, and the asthma, if it develops, is controlled by adrenalin chlorid. If, however, the asthmatic is sensitive to horse-serum, a subcutaneous injection of as small an amount as 0.25 c.c. of antipneumococcus serum will produce violent asthma. Such a patient may be desensitized and protected against horse-serum by frequently repeated gradually increasing doses of horse-serum given first subcutaneously and later intravenously, so that the patient may be given 60 c.c. or more of antipneumococcus serum intravenously before symptoms of asthma appear. This method of desensitization with horse-serum protects against horse-serum for many weeks, but it protects against horse dandruff proteins for only a day or two, indicating that injections of horse-serum are of little or no value in the treatment of horse asthma. The sensitization of patients to different tissues or fluids of the same animal also varies. Taking, for example, the beef animals, the

same patient may be sensitive to any one alone or to any combination of the following tissues or fluids, namely, meat, milk, serum, and hair. Patients differ in their sensitization to the individual proteins of the same cereal, for instance, the same patient may be sensitive to any one alone or to any combination of the individual proteins of the wheat kernel; such proteins, however, are too closely related to be called multiple sensitization. Even the amino-acids give a positive skin reaction.

Multiple sensitization is very common, and such cases are the most difficult to treat. Thus it is seen that it is necessary to test the patient with an almost unlimited number of proteins before one can say that that patient is not sensitive to proteins. For practical purposes, however, such an outlay of proteins is not necessary, since the majority of sensitive patients with bronchial asthma are sensitive to the proteins of horse dandruff, Staphylococcus pyogenes aureus, wheat and other cereal flours, the pollens, Staphylococcus pyogenes albus, cat hair, and egg, all of which have been named in the order of frequency of sensitization. A few patients are sensitive to the protein of milk, feathers, chicken meat, beef, potato, and wool.

We will not describe the methods of isolating and preparing the various proteins, since such proteins are on the market and may be purchased from manufacturers. When such proteins are not available the crude substances may be used in the skin test; for instance, uncooked egg, flour, etc., a 12 per cent. alcoholic extract of animal hair and of pollens, a weak alkaline extract of dried bacteria.

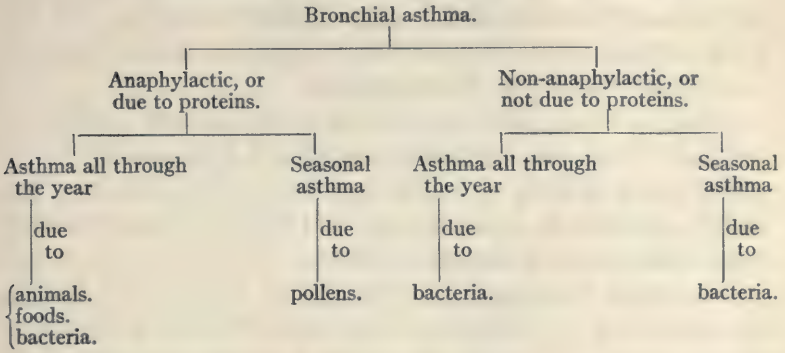
With the exception of bacteria, negative skin tests with proteins rules out those protein substances as a cause of asthma, and a positive skin test with a protein should make one suspect that protein as a cause of asthma. Frequently one meets with a patient who gives a positive skin test with some protein, but at that particular time that protein may not be the cause of asthma; however, at some previous or future time that protein probably has been or will be the cause of asthma, and, consequently, that protein should be eliminated. No patient that had onset of asthma after the fortieth year of age has given a

positive skin test, and one-half of the sensitive patients began to have asthma previous to the age of twenty; quite opposite to these statements is the fact that 40 per cent. of the non-sensitive patients had onset of asthma after the fortieth year of age, and only 15 per cent. had onset of asthma previous to the age of twenty. These statistics thus seem not only to separate bronchial asthma into two types, namely, a sensitive and a non-sensitive, but they are of value in determining the cause and the treatment of bronchial asthma. For instance, the patient that has onset of bronchial asthma early in life is usually sensitive to some protein, and the patient that has onset of asthma after the age of forty is not sensitive to proteins, and in the latter chronic bronchitis is almost always a complication or cause, and cardiorenal disease is frequently a complication or a cause of asthma.

In the case of bacteria, besides the protein element which will be excluded or included as a cause of asthma by the skin test, we have the infectious and inflammatory element entering into the cause of asthma. In discussing the importance of a careful history from the patient we emphasized the relation of asthma to colds, bronchitis, and infections; thus such a history would lead one to suspect the bacterial cause of asthma even though the skin test was negative to bacterial proteins. Obviously, a careful search for bacterial foci should be made with each patient, and such foci are frequently found in the teeth, tonsils, throat, etc. Naturally, cardiac disease, renal disease, and other pathologic conditions must be excluded as a cause of asthma.

From a careful history of the patient and the employment of the skin test we may classify the causes of bronchial asthma. Although such a classification is not infallible, it serves as a good working basis.

CLASSIFICATION OF CAUSES OF BRONCHIAL ASTHMA



We will now present 6 patients with bronchial asthma. The first 3 patients illustrate sensitization to proteins (Case 1 to horse dandruff, Case 2 to foods, Case 3 to bacteria) causing asthma throughout the year; we will not present a case of summer asthma due to pollens, since this type of case is readily recognized. The second group of 3 patients are illustrative of the non-sensitive type of asthma, and bacteria was the cause. Case 4 illustrates the all-the-year type of asthma due to bacteria, Case 5 illustrates another all-the-year type of asthma due to bacteria, but associated with bronchitis in a patient who has cardiorenal disease, and Case 6 illustrates the seasonal type of asthma due to bacteria.

BRONCHIAL ASTHMA CAUSED BY AND TREATED WITH PROTEINS

CASE 1.—D. G., a maid aged twenty-two, began to have asthma one year ago. The first attack was two weeks after an injection of antitoxin. At first she had asthma nearly every night, but shortly the attacks became periodic, although she was never free from asthma for more than a month. Since the onset of asthma the patient has taken cold easily, has had a cough all of the time, and has much expectoration. The patient has lost 30 pounds in weight, is very weak, cannot walk upstairs or on a level for any distance without having asthma. She cannot lie down without wheezing. At times she has raised bloody sputum

and was thought to have tuberculosis, but repeated examinations of her sputum have failed to reveal tubercle bacilli. She has asthma when riding behind horses, but previous to the injection of antitoxin horses gave her no trouble.

Skin reactions were positive with an alcoholic extract of horse dandruff; the coagulated protein of horse dandruff was positive in a dilution of 1 : 100, and the alkali metaprotein was slightly positive in a dilution of 1 : 100,000. The protein of horse-serum gave a negative test.

Treatment was begun on September 8, 1916, with 2 minims of a dilution of 1 : 1,000,000 of horse dandruff alkali metaprotein subcutaneously. The following week 5 minims were given, and after this the patient was able to lie down without wheezing. For the next four weeks treatment was continued with gradually increasing amounts of this protein dilution. The patient was now free from wheezing, had less cough, and less expectoration. On October 27th the dilution of protein was changed to 1 : 100,000, and of this 2 minims were given. The patient was now able to walk up hill without wheezing. The next week 4 minims of this dilution were given; a few hours later the patient had a bad cough, asthma, and had to sit up in bed and gasp for breath. Her arm was very sore. It is noted that the last treatment was double the amount of protein which was given the previous time, and evidently this sudden increase caused the bad attack of asthma. On November 10th the second previous dose, namely, 2 minims of the protein in a dilution of 1 : 100,000, was given. The next week the amount was increased to 3 minims, and a week later it was increased to 4 minims. No inconvenience was experienced this time, even the arm was not sore, so that by gradually increasing the dose of protein no trouble resulted, but following a doubling of the previous dose a severe reaction resulted. The patient was now feeling stronger and was able to walk to the street car two miles distant. Five more weekly treatments were given subcutaneously with this dilution of the protein. At the end of this time the dilution of the protein was changed to 1 : 10,000, and each week the dose was gradually increased until ten doses had been given. The patient now felt

perfectly well, and had gained 32 pounds in weight. She was able to ride behind a horse without having asthma. During the next three months treatment was continued with gradually increasing amounts of a 1 : 1000 dilution of the protein, and finally four treatments were given with a 1 : 100 dilution. At this time the protein which previous to treatment had given a positive skin test in a dilution of 1 : 100,000 now gave a negative test with a 1 : 100 dilution. The patient has continued free from symptoms. Treatment was discontinued. Four months later the patient reported that she still continued to be free from symptoms.

Discussion.—Since the onset of asthma in this case was during early adult life, we would suspect that it was caused by some protein, but not by a food protein, and, furthermore, the patient did not have eczema. On the other hand, the severity of the bronchitis as evidenced by cough, much expectoration which at times was bloody, marked loss of weight and strength, all of which had pointed to tuberculosis, would lead one to suspect that bacterial infection might be the primary cause of asthma rather than a secondary cause, as it was proved to be. In order to treat the patient with horse dandruff protein it was necessary to do skin tests with a series of varying dilutions of the protein to find out what amount of the protein could safely be given to the patient. Since a dilution of 1 : 100,000 of the protein gave a positive skin test, and the next higher dilution gave a negative skin test, it was safe to begin treatment with the latter dilution. The importance of slowly increasing the desensitizing dose of protein is shown. While the amounts of protein were slowly increased the patient had no trouble and improvement was steady; however, when a sudden increase in the amount of protein was given (as occurred on November 3d) asthma followed a few hours later. The rapid improvement of the patient while under treatment is very striking. When the skin tests became negative with horse dandruff proteins treatment was discontinued and four months later the patient was still well.

Case 2.—G. B., a girl aged seventeen, first had spasmodic asthma at eighteen months of age and it continued for years.

In recent years she has had continual asthma and bronchitis with much cough and expectoration. Because of constant wheezing which is aggravated by exertion the patient goes out of doors very little. She has had eczema since six months of age.

The patient's mother and a brother had asthma at three years of age and a maternal grandmother and a paternal uncle had asthma.

Skin reactions were positive with alcoholic extracts of horse dandruff, cattle hair, and wool, with the protein of Staphylococcus pyogenes aureus and albus, with the pollen of red top, timothy, ragweed and golden-rod, and with the various proteins of wheat.

The patient was given subcutaneously 3 minims of whole wheat protein in a dilution of 1 : 500 and much improvement followed. Following 8 minims of this dilution given a week later she was much worse. The next week only 5 minims were given and she had a good week; this was repeated a week later and she became free of wheezing. All treatment was omitted and the patient was put on a wheat-free diet. She began to gradually improve and during the third week she became free from asthma and eczema was improved. The following week by mistake the patient ate some wheat and had a relapse of asthma. After avoiding wheat again for a week she again began to improve until she became free of wheezing. A second time the patient ate wheat without knowing it, until after it was too late, and she had another relapse. Finally, the patient went four months without eating wheat and she became free from wheezing and her cough and eczema were improved. Since she continued to have considerable bronchitis, the patient was given for two months an autogenous sputum vaccine and during this time cough and expectoration gradually decreased. Since the patient was sensitive to pollens, it was essential to desensitize her against them. Therefore during April and May the patient was treated with the pollen of red top and timothy and during June and July with the pollen of ragweed and golden-rod. The patient went through the summer without asthma and she had only a slight bronchitis.

Discussion.—This case illustrates the very early age of onset of asthma from foods and the association of eczema. It also illustrates multiple sensitization. Since the patient became free from asthma when wheat was omitted from the diet, it would seem that wheat was the primary cause of asthma and that the other proteins to which the patient was sensitive played no part at the present time. The case well illustrates the difficulty in keeping anyone on a wheat-free diet and the difficulty in attempting to desensitize a patient with wheat proteins. Although the patient was relieved of asthma and wheezing while wheat was omitted from the diet, she still continued to have bronchitis which was greatly improved by vaccines. On comparing this case with the former one we note that in the former both asthma and bronchitis were relieved by protein treatment, but in the latter only asthma was relieved and the bronchitis required vaccine treatment.

CASE 3.—M. L. S., a dressmaker aged thirty-one, was subject to colds and bronchitis in childhood. Since the age of twelve the patient has had attacks of asthma with colds. At first she had four attacks of asthma each year, one in the fall, one in the spring, and two in the winter. Later she began to have indigestion and gas on her stomach, with attacks of asthma, and she thought that certain foods caused this indigestion and asthma. During the past few months she has had headache and vomiting with attacks of asthma which now come more often at night. Cold air, dust, wind, and exertion provoke wheezing, and asthma and menstruation seem to come together. She has to burn an asthma powder every day or night, and frequently several times.

The patient's brother and a maternal first cousin have asthma and her maternal grandmother had asthma.

Skin reactions were positive with the protein of Staphylococcus pyogenes aureus, all other proteins were negative.

Treatment was begun with 200,000,000 of stock Staphylococcus pyogenes aureus vaccine, a week later 350,000,000 were given, and two weeks later 500,000,000 were given. Following each of the last two treatments the patient had wheezing for two days, so that the amount of vaccine was reduced to 200,000,-

000. During the next two months the patient was given at weekly intervals gradually increasing amounts of this vaccine, beginning with 200,000,000 and ending with 1,000,000,000. During this time she had no wheezing or asthma, she was free from indigestion, was able to work every day, and dust, wind, and exertion caused no trouble. Treatment was discontinued and the patient remained free from all symptoms for three months. At the end of this time she had a severe cold with asthma, cough, and much expectoration. Treatment was begun again with stock Staphylococcus pyogenes aureus vaccine and was continued as previously for four months. During the first month of treatment she had slight wheezing at times and cough and expectoration gradually decreased; during the last three months of treatment she was free from all symptoms. Nine months later the patient reported that she had been free from asthma all this time.

Discussion.—This case illustrates asthma associated with colds and bronchitis in a young adult who had a previous history of frequent colds and bronchitis for years. Since the patient was sensitive to the protein of Staphylococcus pyogenes aureus, stock vaccines of this organism were given, and during such treatment the patient became free from asthma, cough, and expectoration, and remained free for five months, during the latter three months of which time she was given no treatment. When asthma returned again with a long-continued cold she was again relieved of it by similar treatment, and she has continued free from symptoms for a year. It is noted that permanent results did not follow the first course of treatment, but a relapse occurred three months after treatment was stopped. Since the second series of treatments, however, the patient has continued free from symptoms for a year. It is interesting that this patient associated asthma with indigestion for which she blamed certain foods, but that successful treatment relieved her of these symptoms even though she ate these same foods. During the first series of treatments the patient did not seem to do well when the vaccine was rapidly increased, but when more slowly increased improvement was rapid.

Treatment with Bacterial Vaccines of Patients Who are Not Sensitive to Proteins.—CASE 4.—K., a woman aged thirty-six, has had asthma for the past four years and is free from it only a few days at a time. She has a constant cough, with much expectoration. Asthma is worse at night when she wheezes so much that she has to have a hypodermic of adrenalin chlorid and has to take aspirin. She requires several pillows at night and slight exertion causes her to wheeze. For a year she was treated with phylacogen vaccines without benefit. She is a little freer from asthma in Boston than in a city where she lives, 40 miles distant; she has spent considerable time in different parts of the South, West, and Southwest without any relief from asthma.

Skin tests were negative with all proteins.

From the patient's sputum was recovered a diphtheroid organism whch was the predominating one in the culture-media.

The patient was treated twelve times at five-day intervals with a stock Staphylococcus pyogenes aureus vaccine in gradually increasing amounts without relief. The patient was then given twelve treatments with the diphtheroid organism which was recovered from her sputum. These vaccines were given at weekly intervals and in gradually increasing amounts from 200,000,000 to 1,000,000,000. After the second treatment the patient became free from cough, dyspnea, and asthma; a week later she dispensed with the extra pillows and with adrenalin chlorid entirely, but she would wheeze a little unless she took 5 grains of aspirin at night. She was practically free from symptoms for nine weeks and treatment was discontinued. After this, treatment was given at irregular intervals for five months, during which time the patient remained practically free from symptoms.

Discussion.—This case illustrates the difficulty in finding a suitable locality where an asthmatic patient may live with freedom from asthma. It also illustrates the specificity in bacteria in the treatment of asthma caused by bacteria, since Staphylococcus pyogenes aureus vaccine was followed by no relief, whereas the predominating organism in her sputum—namely, a diphtheroid—was followed by comparative relief from symptoms.

CASE 5.—J. G., a housewife aged fifty-two, began to have asthma ten years ago at menopause, with a bad cold. Previous to the onset of asthma she had had bronchitis for years. She has asthma every night, requires several pillows, and has to burn an asthma powder several times each night. Asthma is worse in damp weather, winds, and after a hearty meal. She coughs all of the time and raises much sputum. Removal of polypi from nose relieved her of asthma for two months. Physical examination revealed a slight myocarditis, a slight trace of albumin and a few casts in the urine, and a systolic blood-pressure of 180 mm. Hg.

Skin tests were negative with proteins. From the patient's sputum was recovered a diphtheroid organism; this was the predominating organism in it.

The patient was treated nineteen times in the same number of weeks with a stock diphtheroid organism which was similar to the one recovered from her sputum. She immediately began to feel better and stronger and her cough and asthma gradually diminished until she was free from asthma after the fifth treatment, and she was free from cough and expectoration after the tenth treatment. She was now able to exercise without trouble. After treatment was discontinued the patient went two months with no asthma and no cough, and she did not have to burn her asthma powder. Four months later she was practically free from symptoms with the exception of some cough and a little choking up at night, so that she burned her powder once a night.

Discussion.—This case illustrates the type of asthma preceded by and associated with bronchitis and cardiorenal disease, although the latter evidently played no part in the cause of asthma, since following vaccine treatment the patient became practically free from asthma. The case also illustrates the frequent history of asthma aggravated by damp weather, winds, and overeating.

CASE 6.—S. C., a housewife aged thirty-seven, has had asthma for sixteen years; first attack followed typhoid fever. She rarely has any asthma in winter, but has bad asthma in summer, usually during June and July. Each attack lasts several

hours, and she has a series of these for two weeks, then she is free for a few weeks, when another series of attacks begin. Changes in the weather, colds, dampness, and exertion cause an attack of asthma. She has lived in England, Canada, and for the past few years in the United States, and she has had summer asthma as usual in all these places; she is, however, free from asthma near the salt water. The patient's paternal grandmother had asthma.

Skin tests were negative with all pollens and with bacterial proteins.

Treatment was begun the first of May with Staphylococcus pyogenes albus vaccine. This organism was chosen for treatment since at this time the patient had much secretion from the nose, and from this secretion a pure culture of Staphylococcus pyogenes albus was obtained. The vaccine was given at weekly intervals during May, June, and July; the amount of vaccine was gradually increased from 200,000,000 the first dose to 1,000,000,000 the last dose. Following the second treatment the patient had an attack of asthma on two days, but during the remainder of the treatment she was free from asthma and running of the nose. Treatment was discontinued, and during the fall the patient reported that she had continued to be free from all symptoms.

Discussion.—This case illustrates the summer type of asthma due to bacteria. She was not sensitive to pollens, and evidently pollens played no part in the cause of her asthma. Since this was the first summer in sixteen years that she was free from asthma during the summer months, it would seem that she had been benefited by Staphylococcus pyogenes albus vaccines; even changes in the weather, dampness, and exertion had failed to cause asthma. Although she had lived in a number of different places she had no freedom from asthma in any of them.

Results of Treatment.—Patients whose asthma is due to the proteins of horse dandruff and cat hair are relieved of asthma by subcutaneous injections of these proteins; the more thorough the treatment, the more permanent is the relief. Patients whose asthma is caused by pollens are usually kept from having asthma

the ensuing season provided a course of treatment is given with the pollen before the approach of the pollen season; such treatment does not ensure permanent relief and it is probably best to treat with pollens each year. Bronchial asthmatics who are sensitive to the proteins of Staphylococcus pyogenes aureus and albus are relieved of attacks during treatment with vaccines of these organisms, and such relief continues for from four to six months after treatment is discontinued; a second course of treatment relieves a relapse quicker than did the first course and relief is more permanent. Bronchial asthmatics who are sensitive to the food proteins are relieved of asthma while such foods are omitted from the diet; subcutaneous injections of the food proteins do not usually increase the tolerance of the patient for them.

Patients who are sensitive only to closely related proteins are the simplest to treat, and those who are sensitive to several types of proteins which are not closely related are the most difficult to treat. This is because at first one cannot judge which protein is the cause of asthma at the present time, and so several proteins may have to be tried before the correct one is used. This multiple sensitization does not detract from the value of the skin reaction, since each of the proteins to which the patient is sensitive may have at some time been the real cause of asthma.

Patients with bronchial asthma associate attacks with dampness, changeable weather, winds, menstruation, indigestion, nervousness, colds, and bronchitis. After treatment with proper proteins these patients become tolerant to such conditions and do not have asthma from such causes. There seems to be two types of colds and bronchitis: one type is anaphylactic, and relief or freedom from this type follows proper protein treatment; the other type seems to be due to bacteria and frequently vaccines prevent and relieve these.

The treatment of the non-sensitive group of asthmatics is no less simple than that of the sensitive group. About one case in six is relieved of asthma by vaccines made from a diphtheroid organism; this particular type of bacteria is chosen for treatment when it happens to be the predominating organism in the patient's

sputum. Frequently patients are relieved of asthma following treatment with vaccines of Staphylococcus pyogenes aureus and albus when these organisms happen to be present in the patient's sputum or nasal secretion in large numbers. Occasionally patients are relieved of asthma by vaccines made from a Gram-negative bacillus (so far not identified) when this organism is the predominating one in the sputum. In one case Friedländer's pneumobacillus was the predominating organism in the sputum, and in this case asthma was relieved by vaccines of this organism. Sicard has relieved several patients of asthma by streptococcus vaccines. Therefore the bacterial causes of asthma are very numerous, and for this reason this type of asthma is difficult to treat properly, since many different types of vaccines may have to be tried before the proper one is found. Since the non-sensitive patients usually have chronc bronchitis, this condition must be treated, and in such cases expectorants are helpful. Bacterial foci must be sought for and, if found, they must be eliminated. Cardiorenal disease also may cause asthma; in some instances, however, the nocturnal dyspnea associated with this disease is not asthma.

No matter what the cause of asthma may be, either in a sensitive or in a non-sensitive patient, adrenalin chlorid 1 : 1000 in subcutaneous doses of 15 minims or 1 c.c. is the most reliable for immediate relief in an acute attack of asthma; rarely is it necessary to give morphin or other such drugs.

CONTRIBUTION OF DR. GEORGE W. HOLMES

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THE EXAMINATION OF THE HEART AND GREAT VESSELS BY MEANS OF THE *x*-RAY

The Value of the *x*-Ray in Checking Up Studies in Percussion; Technic.

IN the *x*-ray we have a fairly satisfactory means for obtaining accurate information as to the size, shape, pulsations, and respiratory movements of the heart. None of this data can be obtained as accurately by any other method of physical examination. The size of the heart as demonstrated by percussion is not sufficiently accurate to be of scientific value. This statement is based on personal observation, and the opinion expressed by clinicians who have made careful studies of the value of the various methods used for obtaining the size of the heart. Percussion errors are due to the fact that the walls of the chest are not flat, and lines of vibrations at right angles to them are not at right angles to the borders of the heart. These errors increase as the chest wall becomes more rounded or the size of the heart increased.

The value of obtaining definite data as to the size of the heart is obvious. Perhaps its greatest help is in determining the value of treatment, and in differentiating between organic and inorganic murmurs. It is also valuable in checking up studies in percussion. In an examination of the heart and great vessels by means of the *x*-ray we should obtain the following data: Size, shape, pulsations of the various chambers. Its movements with respiration, changes which may take place with change in the position of the patient, and the size and shape of the aorta

both in the anteroposterior and lateral diameters. The relative position of the diaphragm also should be recorded.

This data may be obtained by the use of parallel rays (orthodiography) or by a combination of teleroentgenography and fluoroscopy examination. Teleroentgenography was introduced

Fig. 192.—The lines outside the heart shadow in this figure represent an area of cardiac dulness as obtained by percussion. Lead markers were placed on the skin previous to the taking of the 6-foot plate. Note the difference in the size and shape of the heart as obtained by the two methods.

by Köhler. Its advantages as compared with orthodiography has been studied by Dietland, and the relative value of the two methods carefully considered. In general, teleroentgenography has the advantage of eliminating the personal equation and of producing a permanent record. Its disadvantages are the

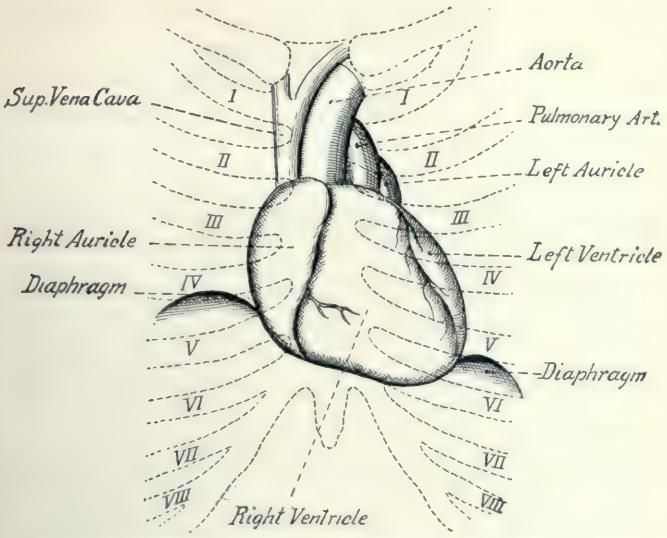

Fig. 193.—The anatomy of the heart in relation to the chest wall. (From Groedel.)

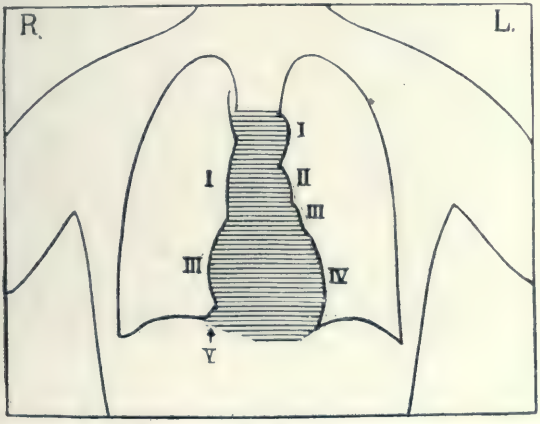

Fig. 194.—This represents the shadow of the heart and great vessels as seen in the anteroposterior view. On the left: I, Prominence of the aortic arch; II, pulmontory artery; III, left auricle; IV, left ventricle. On the right: I, Ascending aorta and great veins; III, right auricle. (From Groedel.)

slightly higher cost and the difficulty of demonstrating the apex of the heart and the junction of the left auricle and left ventricle, which points are of importance in making measurements. There

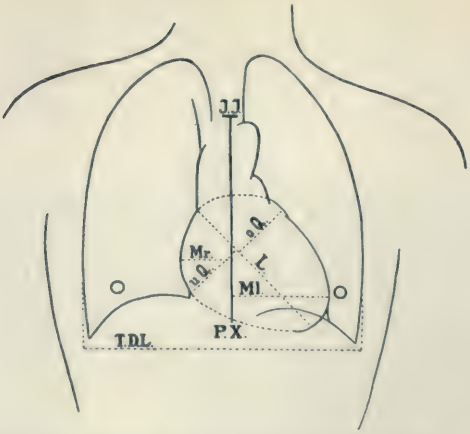

Fig. 195.—The points from which the measurements are obtained. (From Groedel.)

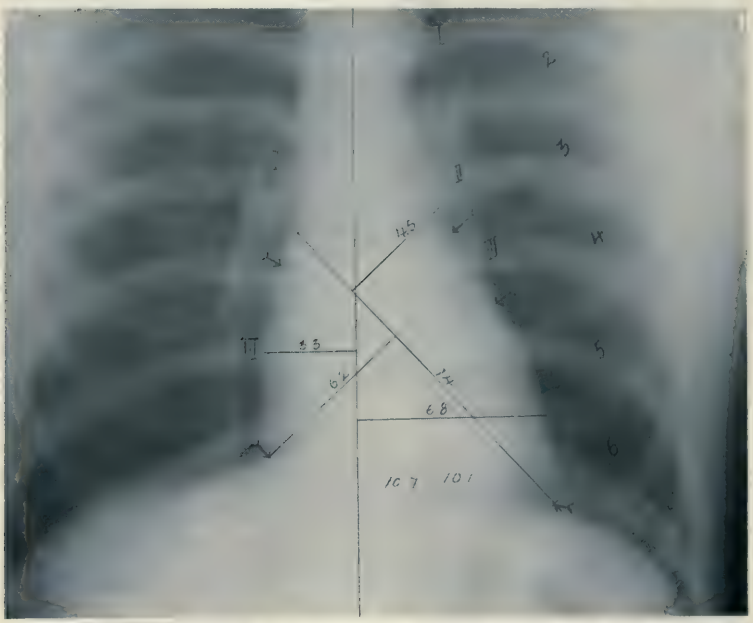

Fig. 196.—Radiograph of a normal heart taken at the tube film distance of 6 feet. The curves of the various portions of the heart and great vessels are indicated according to Fig. 194.

also may be considerable error if care is not taken to prevent rotation of the patient. The plates should be at right angles to the central ray from the tube, which should pass through the antero-posterior diameter of the chest at about the middle of the heart shadow.

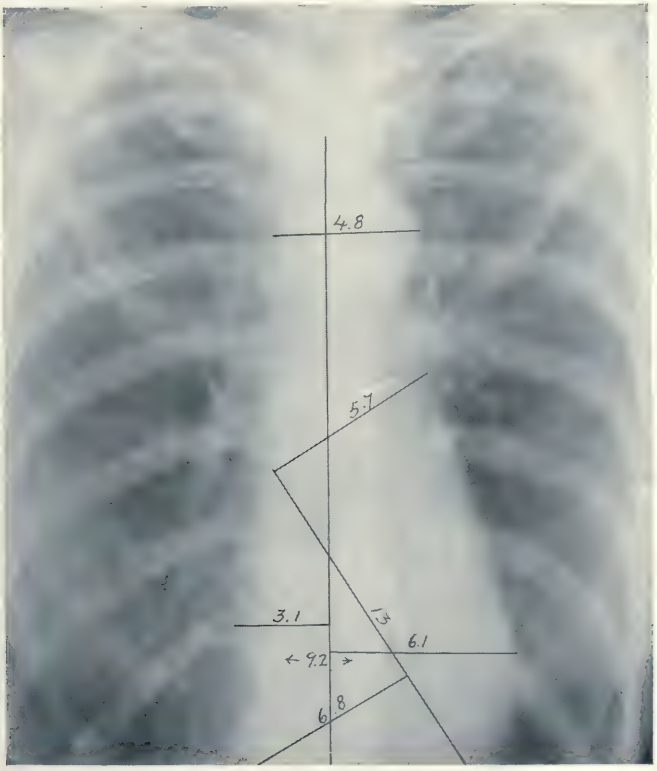

Fig. 197.—Ptosis of the heart and diaphragm; so-called "droop heart."

Orthodiography or the use of parallel rays has the advantage of being slightly more accurate when used by experts, considerably cheaper, and by it the junction between the left auricle and ventricle can be demonstrated. Also in a considerable percentage of cases the apex can be outlined. Its disadvantages are the amount of training required by the operator before his work becomes accurate and the fact that the

personal equation must enter to some extent into every case examined.

By fluoroscopy it is possible to obtain a fairly accurate outline of the shape and position of the heart shadow, its movements with respiration, and any change of shape which may occur with change of position. By combining this data with the data obtained from a plate taken at a distance of 6 feet, all the possible

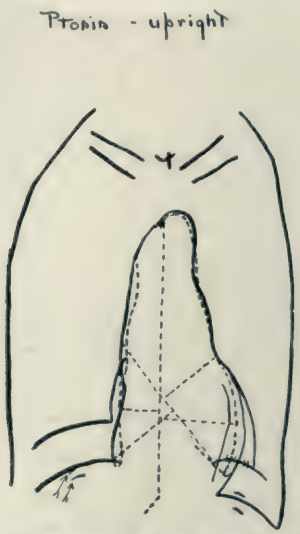

Fig. 198.—Tracing of the heart and diaphragm common in ptosis. The short lines indicated by arrows represent the excursion of the diaphragm during normal breathing. The long lines parallel to them represent the position of the diaphragm during forced inspiration and expiration. Notice that there is no downward excursion of the diaphragm during forced breathing, and that the upward movement in expiration is greater than normal.

data to be obtained from an *x*-ray examination of the heart is secured.

The following technic has been developed and used by us during the past five years, and has been found quite satisfactory: The examination is made preferably in the upright position. A fluoroscopic study is first made with the tube at a distance of 2½ feet. At this distance very good illumination of the chest can be obtained with a small amount of current. The respiratory

excursion of the diaphragm and the outline of the heart and great vessels are observed and tracings made on glass, which is later transferred to a chart (Fig. 210). Observations are made as to the rapidity, force, and time of the pulsations in the various chambers. The positions for obtaining the preceding data are the antero-posterior and right oblique. Where aneurysm is found or suspected, it may be necessary to use the left oblique and lateral

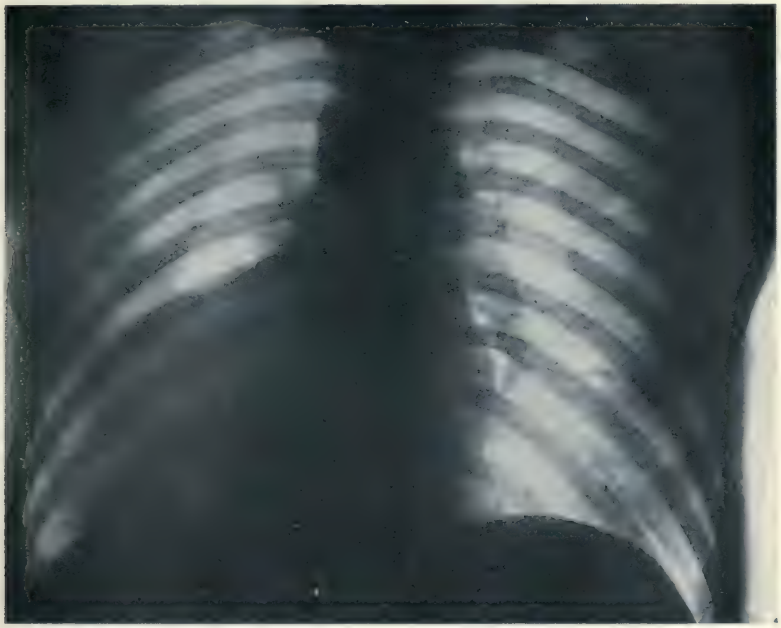

Fig. 199.—Aortic regurgitation with hypertrophy of the left ventricle. This plate was taken at a distance of 2 feet, with the patient in the upright position.

views, or examination in the prone position if fluid in the pericardium is suspected. After completing the fluoroscopic observations, and marking on the chest wall a point opposite the central portion of the heart shadow, the plate with the target of the tube at a distance of 6 feet is made. Intensifying screens are used. The exposure is long enough to include a full heart cycle, thereby obtaining the shadow of the heart in diastole.

The patient is not asked to take a deep breath or to hold the

breath. The amount of change in the size, shape, or position of the heart during normal breathing is very small, whereas the change in forced inspiration or expiration is considerable, and as it is not usually possible for patients to take the same depth of breath on different occasions, comparison of results would be impossible. It is particularly important that the central rays

Fig. 200.—Same patient as Fig. 199. The plate, however, was taken at a distance of 6 feet. Note that in Fig. 199 there is not only magnification of the heart shadow but also distortion of the shape. Figure 197 shows the typical appearance of the heart outline in aortic disease.

from the tube pass through the chest in a plane at right angles to the transverse diameter of the chest. If there is rotation of the patient the shadow of the heart will be changed both in size and shape. This can be avoided by care in placing the patient for the examination. The plate or screen should lie on the anterior chest wall. In stout people it is better to tilt the plate than to have the patient lean forward or to allow the upper portion of

the plate to be at a considerable distance form the chest wall, as this tends to distort the shadow of the upper part of the heart and great vessels. A tube of fairly high penetration should be used with a moderate amount of current. The length of the exposure may be from five to twenty seconds.

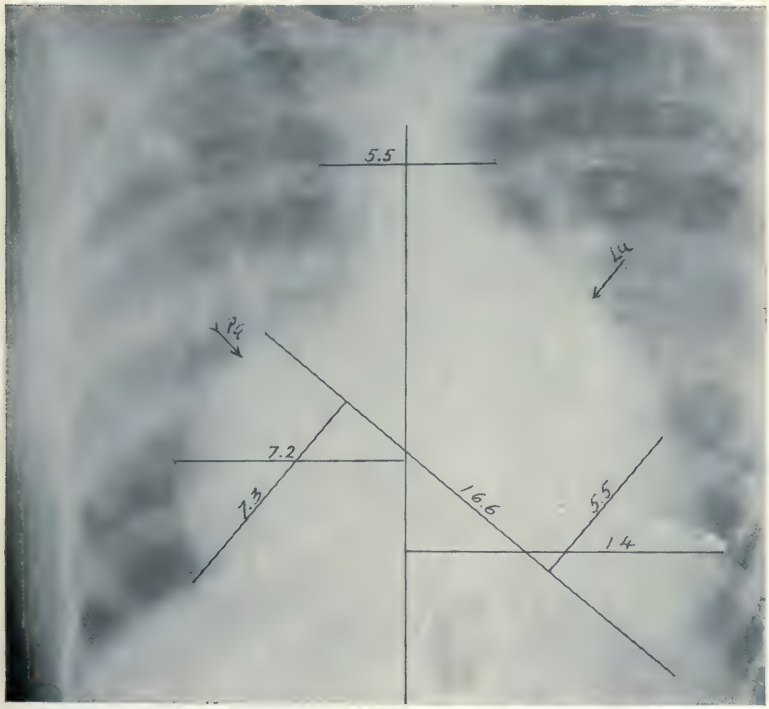

Fig. 201.—Mitral disease, regurgitation, and stenosis. Note the marked prominence of the heart shadow in the region of the right and left auricles. Compare its appearance with Figs. 196 and 200.

In order to interpret the findings it is necessary that the observer have a working knowledge of the *x*-ray anatomy of the chest. The shadow of the normal chest is composed of the thoracic wall, a central shadow composed of the superimposed sternum, heart, great vessels, mediastinum and spine, the diaphragm, and the lung fields. Normally the central shadow should approximate Fig. 196. At the top of the left side the edge of the arch

of the aorta appears with the descending aorta extending downward from it. Next comes the slight prominence of the pulmonary artery and the small prominence of the auricle, below which is the rounded mass of the left ventricle, making up the larger part of the shadow on this side and disappearing below the line of the diaphragm. On the right, above, the edge of the shadow

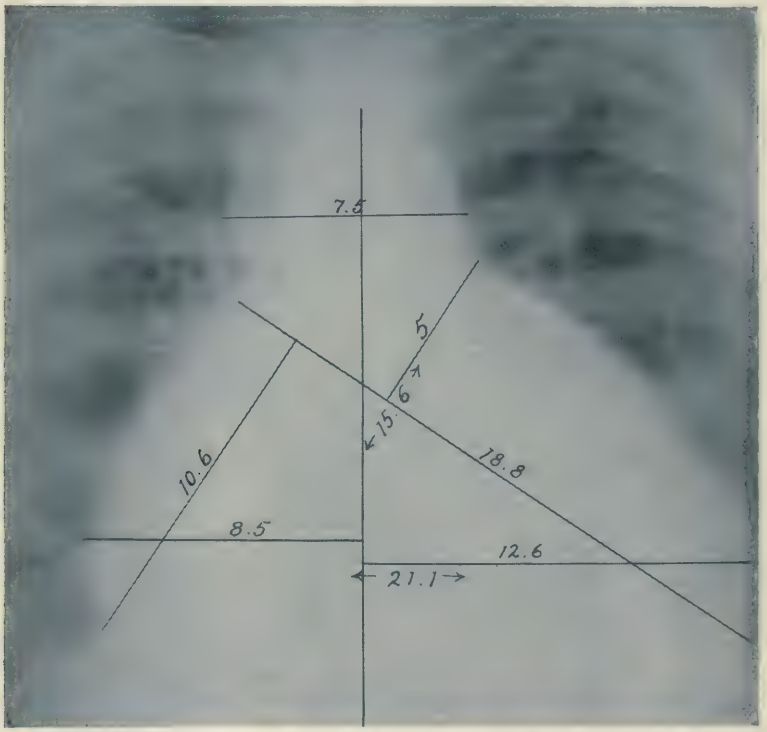

Fig. 202.—General enlargement of the heart shadow due to dilatation.

is formed by the ascending aorta and great veins, below is the curve of the right auricle which joins the right ventricle near the line of the diaphragm. The right ventricle is usually not seen, as it lies in front of the mass of the heart.

The shadow of the pericardium is not distinguishable from that of the heart unless it is calcified or contains air. Patho-

logic processes in the lungs or pleura may displace or distort the shadow of the heart and great vessels. The change in position of the diaphragm will also produce changes in the shadow of the heart. Diseases of the heart valves are accompanied by an enlargement of the shadow of the corresponding chamber or chambers. For instance, in mitral regurgitation we have en-

Fig. 203.—General enlargement of the heart shadow due to fluid in the pericardium, taken with the patient in the prone position, tube film distance 6 feet. Note that the shape of the shadow is roughly triangular and that the cardiohepatic angle is not obliterated. Compare with Figs. 202 and 204.

largement of the shadow of the right auricle and right ventricle. A knowledge of the physiology and pathology of the heart will enable one to interpret quite accurately these lesions from the changes in the shape of the heart shadow. Auricular fibrillation may be determined by the tremendous enlargement of the shadow of the auricles and the absence of visible pulsation. In heart-block if the pulsation is not too rapid it is possible to com-

pare the beats of the auricle with those of the ventricle and determine their respective rapidity. Dilatation is seen as a general enlargement of the heart shadow with weak pulsation and an absence of the rounding of the apex seen in the hypertrophied heart. Congenital abnormalities of the heart give rise to changes

Fig. 204.—Same patient as Fig. 203, tube film distance 6 feet; patient in the upright position. Notice that the shadow has assumed roughly the appearance of a water-bottle. The lower part of the shadow has increased; the upper part diminished, due to the shifting of fluid in the pericardium. Compare with Fig. 203.

in shape and abnormal areas of pulsation. Here again the knowledge of the *x*-ray anatomy and the pathology of the heart and great vessels will enable one to arrive at a diagnosis.

Fluid in the pericardium tends to give a triangular shaped shadow. When prone there is an increase in breath of the upper portion or apex of the triangle. When upright it may assume a

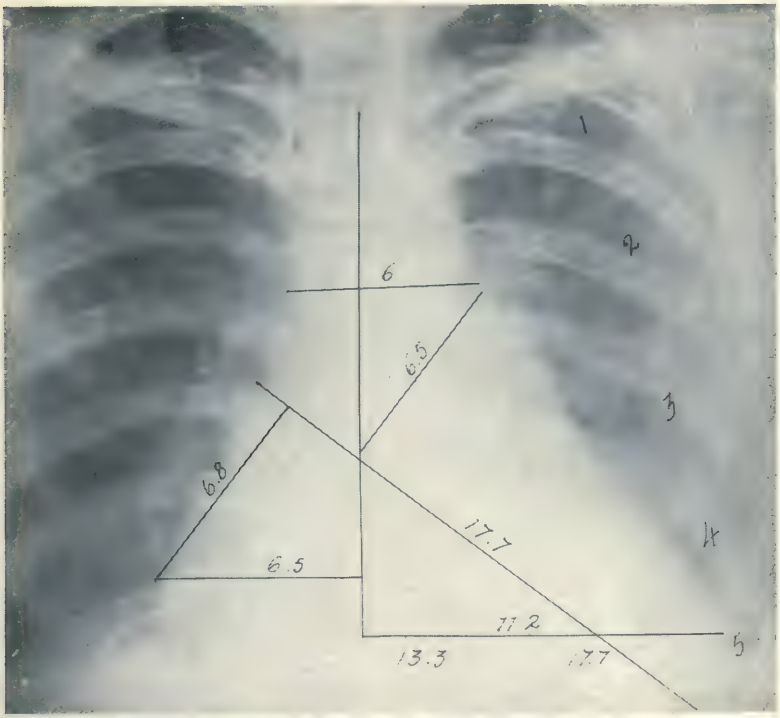

Fig. 205.—Adhesive pericarditis. Notice that the heart shadow is roughly triangular and that its outlines in the lower portion are rather indistinct.

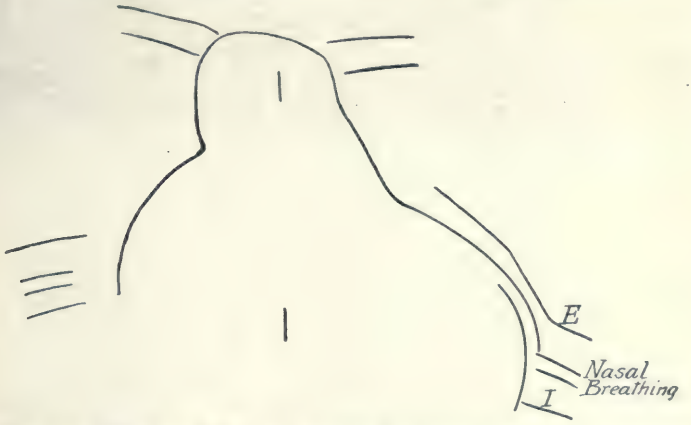

Fig. 206.—Tracing of Fig. 205, showing the limited respiratory excursion of the heart. The lines marked with the arrows represent the positions of the left border during forced breathing.

water-bottle appearance. The cardiohepatic angle is not necessarily obliterated, although it may be so to percussion. Pulsation is considerably diminished or absent. In obtaining the shape of the heart in the different positions for comparison it is not wise to depend on screen observations alone; either a careful tracing or plate taken at a distance of 6 feet should be made, and the outlines thus obtained superimposed.

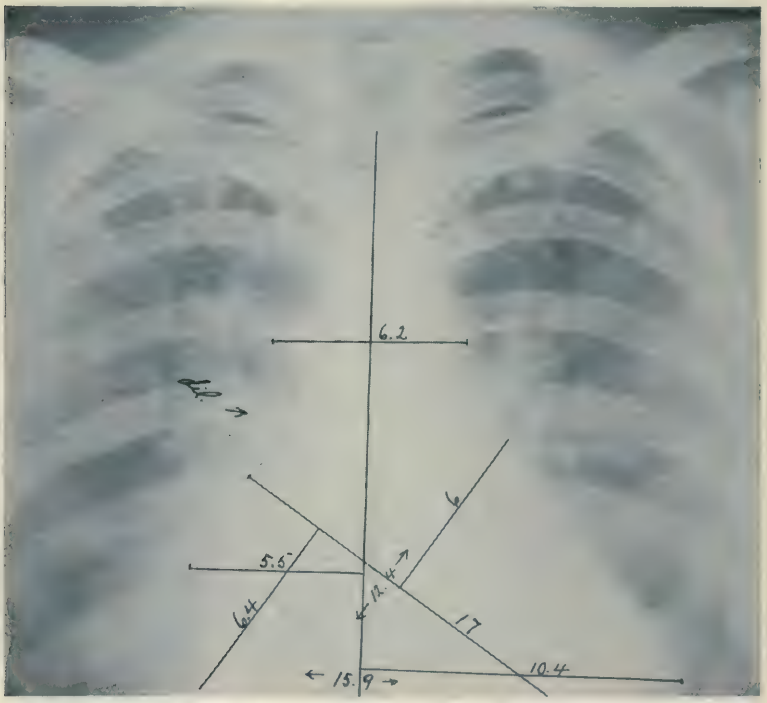

Fig. 207.—Specific aortitis proved at autopsy. Note the prominence of the first portion of the aorta as indicated by the arrow.

Adhesive pericarditis may prevent to a certain extent the respiratory movements of the heart. Figures 205 and 206 illustrate such a case which was proved at autopsy. The shape of the heart shadow is not necessarily changed in this disease, but its outline is usually less distinct, as are also the pulsations. Changes in the shadow of the great vessels may be due to dilata-

tion, arteriosclerosis, or aneurysm. Dilatation of the aorta may be of the ascending, transverse, or descending portion, or it may be diffuse. It has been shown that in a considerable percentage of cases of specific aortitis the lesion occurs near the aortic valve, and that this portion of the aorta is the first to become weakened. Therefore in this type of case we should expect to see a bulging

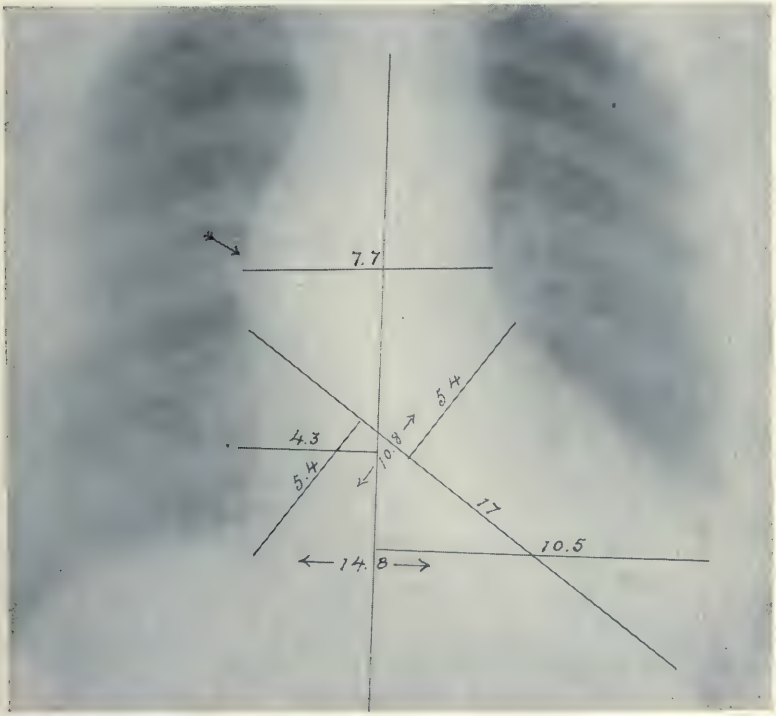

Fig. 208.—Specific aortitis with marked prominence of the first portion of the aorta; possibly beginning aneurysm.

of the shadow of the ascending aorta on the right side just above the right auricle. A case proved at autopsy is illustrated in Fig. 208. Where the process is more general, the findings are shown as an increase in the transverse diameter of the shadow of the great vessels. Differentiation between a marked dilatation and a small aneurysm is not always possible. Usually, however, the aneurysm appears as a dense, sharply defined mass pro-

jecting from the shadow of the great vessels. Pulsation may or may not be visible. Its position, right, left, or central, will depend upon whether or not it rises from the ascending, descending, or transverse portion of the arch.

Arteriosclerosis is shown by a wider curve to the arch, noticeable as a prominence high on the left. It is not usually possible to demonstrate the presence of calcification in the aorta.

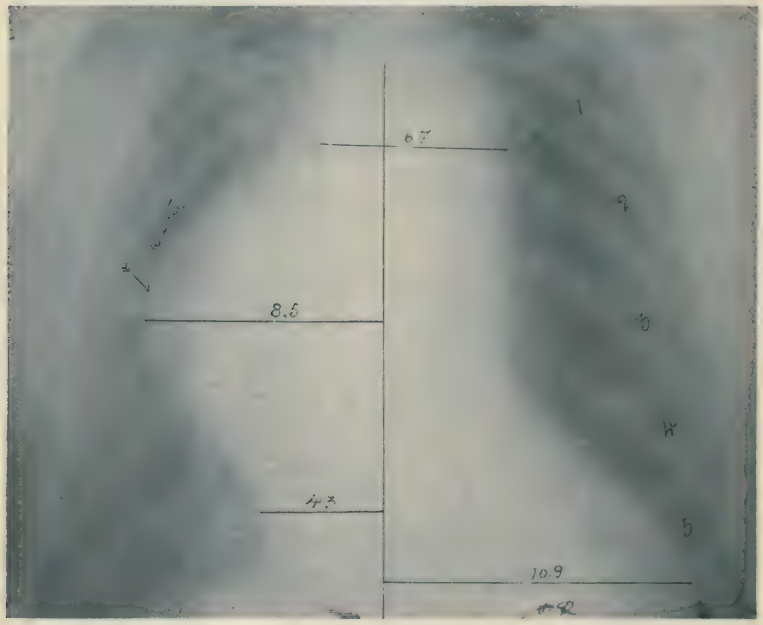

Fig. 209.—Aneurysm of the ascending portion of the aorta.

The methods of examination used in this clinic, while not entirely free from errors, are sufficiently accurate for all practical purposes. In conclusion I wish to emphasize the necessity of the 6-foot target film distance for obtaining the plates from which the measurements are taken, and of making the exposure during normal breathing. Accurate measurements cannot be obtained from plates made with shorter tube distance, because the amount of magnification of the heart shadow due to divergent rays depends not only upon the distance of the source of the rays from

it but also upon the distance of the heart from the plate and upon its size. It is therefore essential that parallel or nearly parallel

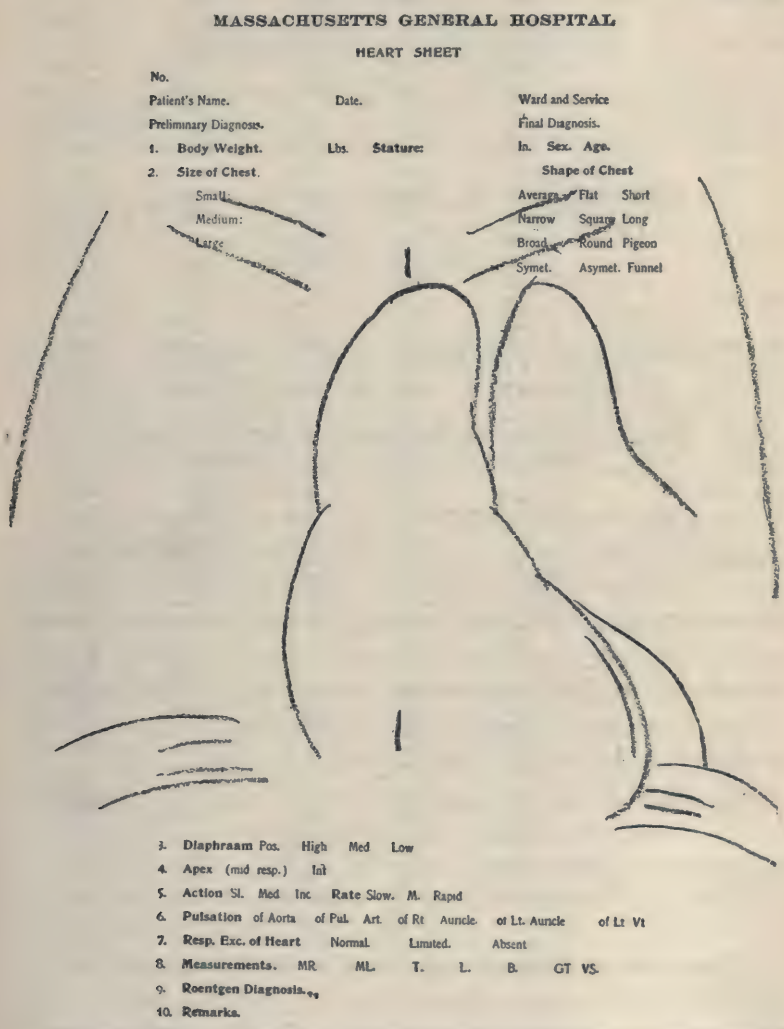
MASSACHUSETTS GENERAL HOSPITAL
HEART SHEET
No.
Patient's Name.
Date.
Ward and Service
Preliminary Diagnosis.
Final Diagnosis.
1. Body Weight. Lbs. Stature: In. Sex. Age.
2. Size of Chest.
Small:
Medium:
Large:
Shape of Chest
Average Flat Short
Narrow Square Long
Broad Round Pigeon
Symet. Asymet. Funnel
3. Diaphragm Pos. High Med Low
4. Apex (mid resp.) Int
5. Action Sl. Med Inc Rate Slow. M. Rapid
6. Pulsation of Aorta of Pul. Art. of Rt Auricle of Lt. Auricle of Lt Vt
7. Resp. Exc. of Heart Normal Limited. Absent
8. Measurements. MR ML T. L. B. GT VS.
9. Roentgen Diagnosis.
10. Remarks.

Fig. 210.—Chart for recording the examination of the heart and great vessels in use at the Massachussets General Hospital. The tracing on it is that of a normal heart. Notice the amount of respiratory excursion of the left side of the heart.

rays be used. Appended is a table (p. 1214) giving the average normal measurements of the adult heart.

CLAYTOR, MERRILL: ORTHODIAGRAPHY

TABLE 1.—Vertical Heart Measurements. Male (37 cases).

Weight, pounds.	Cases.	Mr.	Ml.	T. D.	L. D.	
		3	7.0	10.7	11.8	Min.
120–129	3	3.7	7.2	10.9	12.6	Av.
		4.3	7.5	11.3	13.5	Max.
		3.5	7.5	11.0	12.0	Min.
130–139	5	3.8	8.0	11.8	13.2	Av.
		4.2	8.5	12.5	14.0	Max.
		3.4	7.0	11.0	12.0	Min.
140–149	9	4.0	7.7	11.9	13.4	Av.
		4.6	8.4	13.1	14.5	Max.
		3.2	7.8	11.5	12.5	Min.
150–159	8	3.9	8.4	12.3	13.5	Av.
		4.5	9.0	13.0	15.0	Max.
		3.7	8.0	12.0	14.0	Min.
160–179	6	4.0	8.2	12.4	14.6	Av.
		4.8	9.0	13.8	15.8	Max.
180–200	6	3.8	7.0	11.0	14.0	Min.
		4.2	8.7	12.9	14.7	Av.
		4.5	9.7	13.4	15.3	Max.

TABLE 2.—Vertical Heart Measurements. Female (54 cases).

Weight, pounds.	Cases.	Mr.	Ml.	T. D.	L. D.	
100–109	2	3.2	6.7	9.9	12.0	Min.
		3.3	6.8	10.2	12.1	Av.
		3.5	7.0	10.5	12.3	Max.
110–119	3	3.0	7.0	10.0	11.5	Min.
		3.1	7.6	10.7	11.9	Av.
		3.2	8.0	11.1	12.4	Max.
120–129	14	2.3	6.4	10.2	10.5	Min.
		3.5	7.5	11.0	12.2	Av.
		4.2	8.6	12.2	13.8	Max.
130–139	19	3.0	6.4	9.6	11.2	Min.
		3.4	7.8	11.2	12.4	Av.
		4.0	8.8	12.6	13.3	Max.
140–149	5	2.6	7.0	10.0	12.2	Min.
		3.5	7.6	11.1	12.7	Av.
		4.1	8.3	11.8	13.2	Max.
150–159	7	3.1	7.6	10.9	12.3	Min.
		3.6	8.0	11.6	12.9	Av.
		4.8	9.3	12.8	14.2	Max.
160–175	4	3.5	6.5	10.6	11.8	Min.
		3.8	7.9	11.7	12.6	Av.
		3.8	8.5	12.3	13.0	Mean.
		4.1	9.0	12.8	13.2	Max.

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NORTH AMERICA

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CLINIC OF DR. CHARLES LOUIS MIX

MERCY HOSPITAL

AORTIC REGURGITATION, AORTITIS, AND ANEURYSM ON A SYPHILITIC BASIS. FUNDAMENTAL PRINCIPLES UNDERLYING THE DIAGNOSIS OF THE MORE COMMON CARDIAC LESIONS

BEFORE taking up the history of the patient to be shown it may be well to consider some of the fundamental principles underlying the diagnosis of the more usual cardiac diseases. If we have a clear conception of these principles, the diagnosis of the individual case becomes comparatively easy. Leaving out of consideration congenital heart lesions and such as are due to disturbances of cardiac innervation, thyrotoxicosis, pericarditis, etc., the great majority of cardiac lesions will be found to divide themselves readily into four great groups—the so-called rheumatic hearts, the syphilitic hearts, the renal hearts, and the arteriosclerotic hearts. This rather simple classification was suggested by Richard Cabot, and affords a most excellent basis for diagnosis in the individual case.

1. **Rheumatic Heart.**—By a rheumatic heart we mean a heart in which the endocardium has been affected by some infectious germ. Although the term "rheumatic" is applied to it, it is really the heart of metastatic infection. Usually it is found in association with tonsillitis and acute articular rheumatism, or it is a sequel of chorea. It may be rather latent in origin, but, as a rule, it begins shortly after a systemic infection of the body. The

germs, finding lodgment primarily in the tonsils, may infect the organism and be carried by the blood-stream to the heart. The organisms are then carried into the coronary arteries and, passing through the finer branches, ultimately reach the vulnerable portions of the cardiac anatomy. It was long since shown by E. A. Rosenow that the most vulnerable point is located just beneath the auricular surface of the mitral valves. Here beneath the upper surface of one or both mitral flaps, where there is, on the whole, the most insufficient blood-supply of any portion of the heart, the germs find their resting-place and begin their nefarious work. They first cause an interference with the working of the valve, permitting a slight amount of leak to take place. This occasions the systolic blow which we hear when we are in attendance upon a case of acute inflammatory rheumatism. The probabilities are that this murmur is due quite as much to interference with the sphincteric action of the auriculoventricular muscle-fibers as it is to deformity of the valves themselves. For a heart the valves of which are inflamed can hardly be expected to act physiologically as perfectly as the heart which has not been maimed. The first effect, then, in any case of mitral disease is to produce a faint systolic blow, heard usually best over the mitral area, and, as a rule, transmitted rather early toward the axilla, though it is sometimes heard even in the back at this stage. As time goes on the effect of the inflammation which the germs set up becomes more and more wide-spread. The result is that the valve becomes very lame in its workings, so that the leak is accentuated.

In the course of time an immunity may be acquired for the infecting germs by the organism and the infectious process may die out. This results, first, in the lessening of the inflammation, and, second, in the establishment of a certain amount of contractile and contracting scar tissue in the valve. The result of the contraction of this scar tissue is to pull asunder the edges of the mitral valve. Thus the leak becomes an organic one and can never be obviated by any kind of treatment. Indeed, it is axiomatic that mitral insufficiency thus resulting will never be cured.

The rheumatic heart may remain healed in this condition and

is permanently healed in a great many individuals whom we examine. These are the cases with the soft systolic blow who go through life with little or no difficulty and never suffer from shortness of breath, palpitation, or swelling of the feet or ankles, and who sometimes ask and obtain insurance from large insurance companies. Such individuals acquire what is called "compensation." The left ventricle mildly dilates and sufficiently hypertrophies. It dilates enough to accommodate sufficient blood to supply the needs of the body and to allow for the regurgitation of a small amount backward into the auricle. It hypertrophies to an extent great enough to propel without effort this increased amount of blood.

In this stage the heart may remain indefinitely, but it not infrequently happens that the process does not heal in the form of a permanent mitral insufficiency, but at a subsequent period a reinfection or recrudescence of the original infection takes place. If so, there is added to the original difficulty an associated mitral stenosis. This is brought about by reason of the fact that a greater amount of inflammation in the auricular valve either fastens the edges of the valves to one another, or leads to a general contraction of the left auriculoventricular septum. Thus, in mitral disease, mitral stenosis is merely an advanced stage of mitral insufficiency. The old authors—von Leube, for example—used to assert that if you make a diagnosis of mitral stenosis, the diagnosis of mitral insufficiency should go automatically with it; that a mitral valve which is narrowed will always be a mitral valve which will leak. The converse statement, of course, was not made, namely, that a leaky valve will become a narrowed one. We all know that leaking valves may remain merely leaking valves, but many individuals find out later in life, to their cost, that a leaking heart has within it the power of becoming a stenosed heart.

In mitral insufficiency a characteristic feature is a comparatively normal pulse. It is scarcely affected by the cardiac lesion. There is no change in the rate, tension, rhythm, or quality. It is neither fuller nor larger, nor emptier nor smaller than a normal pulse. It deviates so little from the normal pulse that even ex-

perienced observers would not by the pulse alone be able to postulate the probable existence of mitral insufficiency. In mitral stenosis this is not true. The pulse is profoundly affected both as to rate, rhythm, and quality. Later investigations have shown excellent reasons for this changed pulse, and this leads us briefly to discuss what we know concerning the mechanism for maintaining cardiac rhythm.

As all medical men now know, the pace-maker of the heart, the sino-auricular node, is located in the right auricle, at the junction of the auricle and superior vena cava. When the auricle contracts, because of the pace-maker, it sends its impulses down the bundle of His in the intraventricular septum. This bundle as it passes down divides in a Y-shaped manner, one portion going to the fibers of the right ventricle and another portion to the fibers of the left ventricle. Thus, an impulse originating in the auricle is carried along the fibers of the bundle of His and ultimately forces into activity the muscular fibers of the ventricles. The time required for the passage of an impulse from the auricle to the ventricle is from one-tenth to two-tenths of a second. The disturbance of this mechanism results in a mild degree of heart-block—the As.-Vs. interval being increased beyond two-tenths of a second.

Late studies made by Paul White have shown that in cases of well-compensated mitral stenosis disturbances of the bundle of His occur in quite a large number of cases, constituting, in reality, a mild degree of heart-block. In mitral stenosis the marked inflammation of the mitral flaps often spreads to the bundle of His and so disturbs the cardiac rhythm; or it may exert a perverted physiologic influence upon it at least. If, for example, we are treating a case of what seems to be pure mitral insufficiency, and we find that without any sign of a break in the compensation the pulse-rate has become rather fast and that there is some departure from perfect rhythm and some variation in equality of the pulse itself, we should be justified in inferring that an extension had probably taken place in the mitral insufficiency case in the direction of the establishment of a secondary mitral stenosis. Before the stage of the well-known diastolic murmur

of mitral stenosis a suspicion of a possible narrowing might be gained by careful pulse examination. The electrocardiogram is not wholly necessary. Estimation can be made usually fairly shrewdly with the cultivated sense of touch.

In the earliest stages, therefore, of mitral stenosis probably the only change that can be detected is the slight variation or tendency to variation from normal on the part of the cardiac rhythm. As time passes on, however, there is added to the picture the presence of a diastolic murmur. This diastolic murmur in an early developing case of mitral stenosis is really a presystolic murmur, taking place at the extreme end of diastole and just before the beginning of systole. It would seem as though the left auricle succeeded in pouring the first portion of its charge of blood through the mitral orifice into the left ventricle without the production of eddies, until ultimately the last remaining portion is forced rather rapidly through the narrowing valve, thus producing eddies in the ventricular blood and so causing a presystolic murmur. It is safe in the presence of a presystolic murmur in the great majority of compensated cases to assume that we are dealing with a comparatively early or first stage case of mitral stenosis.

In the course of time, when the narrowing of the valve becomes greater, the murmur stretches backward into diastole and the pulse becomes rapid, habitually arhythmic and unequal, and the murmur becomes frankly diastolic in point of time. Ultimately in some cases of a so-called third degree of mitral stenosis the opening between the valves becomes so narrow as to be hardly more than a buttonhole slit, the approach from the auricle through the valves into the ventricle being almost funnel shaped by reason of the changes which have taken place in the mitral flaps. When this stage is reached there is usually marked anatomic or physiologic involvement of the bundle of His, so that one finds in such cases very marked arhythmia and inequality, and frequently the evidence of heart-block, either in the sense of a lengthening of the As.-Vs. interval, or in the sense that there is an occasional absolute omission of the ventricular beat. These facts as to the pulse can often be picked up by the

finger if one is on the lookout for them. I do not mean to say that it is possible to diagnose heart-block by a sense of touch, but I do think it is possible in certain instances to suspect its presence with confident certainty.

Those of you who are conversant with older medical literature will remember that years ago it was taught by empirical therapeutists, notably Wood, that digitalis, while an excellent remedy in cases of mitral insufficiency, is contraindicated in cases of mitral stenosis. The work done by the physiologic therapeutists in the last few years on digitalis established the fact that it is of value in both cases, but the more recent work has led to the dictum that digitalis is contraindicated in heart-block. Inasmuch as in a certain proportion of mitral stenosis cases—possibly as many as 20 per cent. of all cases—heart-block exists, it is evident that Wood was right in insisting upon the valuelessness of digitalis in mitral stenosis in a certain proportion of his cases. Indeed, as the therapeutists know, strophanthus in mitral stenosis is apt to be far more valuable than digitalis. Although digitalis may work beautifully in some cases, in others it will not work at all. It will work in those cases alone in which there is no involvement of the bundle of His. It will not work in those cases in which there is such involvement.

In the "rheumatic" heart, then, you invariably have an inflammation which in the beginning affects the auricular surface of the valve-flaps, and which goes on to the production of an organic mitral insufficiency. It may stop at this point, heal up, and remain without further change during the individual's life, or the infectious process in the valve may light up afterward and go on to the production of mitral stenosis. The mitral stenotic disturbance may end in the first stage, in which there is merely a very slight presystolic murmur, or it may proceed to the second stage, in which there is a diastolic murmur, or to the ultimate third stage, in which there is a marked arhythmia, marked inequality of the pulse, rapid heart action, and great tendency toward passive congestion, especially of the lung and liver, and broken compensation, with secondary tricuspid insufficiency.

This is the picture of the rheumatic heart. It occurs in young individuals, and we do not expect to see it develop in people who have reached the fifth decade of life. We expect to find it in children who have had St. Vitus' dance or in young adults who have had tonsillitis repeatedly, or inflammatory rheumatism, or metastatic arthritis of one sort or another. We rarely ever expect to encounter it in later life, and if we think we do encounter it, we examine such suspects with the utmost care, because the probabilities are that we are mistaken. It is possible, then, almost at a glance, noting the age of the individual and his general appearance, to say that he, if he has organic cardiac disease, is more likely to be suffering from a rheumatic heart than from a renal, arteriosclerotic, or syphilitic heart.

Many of these rheumatic hearts do not stop merely with the development of mitral insufficiency and stenosis, and possibly at times tricuspid insufficiency, but in many of them the aortic valves also become affected. When they do, the flaps of the aortic valve go through precisely the same pathogenesis as the mitral valve. Aortic insufficiency first develops and it may persist indefinitely. The valves may definitely heal in this stage and no further trouble ensue, but, as in the case of the mitral valve, it very commonly happens that the process does not quiet down with the production merely of an aortic insufficiency, but goes on to the production of an associated aortic stenosis. Thus many a rheumatic heart is found to have all four valvular lesions with all four murmurs, a double mitral and double aortic lesion.

When in a rheumatic heart an aortic insufficiency develops, it does so almost invariably as a sequel to disturbance of the mitral valve. Although it is possible for primary rheumatic aortic insufficiency to occur with the preservation of the integrity of the mitral valve, still such an event is an extremely rare one. Almost invariably it happens that the mitral valve is first affected, then the aortic valve becomes secondarily affected. Just as when the mitral valve is affected the insufficiency first appears, so when the aortic valve is affected the aortic insufficiency first appears; but since this aortic insufficiency on a rheumatic basis in the vast

majority of cases occurs in the presence of an associated mitral insufficiency and stenosis, it happens that the picture of aortic insufficiency departs very much from the classical description. This brings me to the assertion that the medical text-book description of aortic insufficiency is not the description of "rheumatic" aortic insufficiency, but of syphilitic aortic insufficiency. Rheumatic aortic insufficiency differs tremendously from syphilitic aortic insufficiency. The two pictures are wholly unlike. In some text-books and by some writers the statement will be made that aortic insufficiency is notoriously missed by internists in their diagnosis; that postmortem examination frequently discloses the presence of aortic insufficiency when it was not diagnosed by the internist in charge. That may have been the case in the past, but it ought not to be the case now. Knowing as we do at present that rheumatic aortic insufficiency in the presence of double mitral disease is invariably atypical, that it never approaches the classical description of syphilitic aortic insufficiency in any manner, we should be on our guard; and, being on our guard, in looking for it we shall more frequently find it than we used to in the past.

When aortic stenosis is added to aortic insufficiency the changes in symptomatology and physical signs which it makes are very marked. Years ago von Leube enunciated three criteria as absolutely essential in the diagnosis of aortic stenosis. These three criteria are: (1) A loud, sawing systolic murmur transmitted upward into the neck; (2) a palpable systolic thrill over the second right interspace; (3) the absence of the aortic second sound. To these three criteria Broadbent added a fourth, namely, that the pulse of aortic stenosis must be a *pulsus tardus et parvus*, a pulse slow, not rapid, frequently not much faster than 60; a pulse in which the anacrotic arm rises very slowly, a *pulsus rotundus* with a round top, and a pulse with a very much diminished volume. If the aortic valve is narrow it is perfectly obvious that the left ventricle cannot deliver its charge of blood through the narrowed aorta as many times per minute as it could if the valve were wide open. It has not sufficient time to squeeze out all of its blood as it would have if the valve were undisturbed. Furthermore, it

cannot squeeze out through a narrow valve an amount of blood great enough to cause a good wave running down through the arteries; consequently, there is a *pulsus tardus et parvus*, slow and small. This pulse is one of the diagnostic essentials, if one is to establish a diagnosis of aortic stenosis.

Aortic stenosis is really a rare lesion. A systolic murmur in the second right interspace, soft in character, instead of loud and sawing, not associated with a thrill, not associated with the absence of the aortic second sound or with the changes in the pulse, is exceptionally common after the fifth decade of life. It never means aortic stenosis; it merely means aortitis. There is no chance for making an error in this respect if one remembers the criteria of von Leube. I do not mean to say that a beginning aortic stenosis must necessarily have associated with it all four of these criteria, but I do mean to say that they should be sufficiently developed in the ordinary case for one to be conscious of their presence, and thus to establish a diagnosis of double aortic lesion.

By way of a summary, then, the rheumatic heart is the heart of a young individual who has had some acute infection from which his cardiac malady is dated. It may be a chorea in childhood, or even a scarlet fever, though this is unusual. It is more frequently a tonsillitis or a "cold," or an acute inflammatory rheumatism. The first sign of its presence is a slight systolic blow heard in the mitral area and transmitted toward the axilla. It is transmitted in this direction because it is made in the left side of the heart, which lies behind the right side of the heart. The murmur cannot come through to the front of the chest because it is padded off by the right side of the heart, which is in front. It can escape, however, up into the armpit from underneath the heart, and so may be transmitted into the back of the chest. Thus we hear such mitral murmurs in two localities, the left axilla and the left back. The patient's heart may heal in this condition. He may for the rest of his life have nothing but the remains of his mitral insufficiency, but, unfortunately, in the great majority of cases an extension of the original disease takes place, and in the course of time, sometimes in a few weeks and

sometimes in a few years, there is added to the original mitral insufficiency a mitral stenosis.

Nor does the process stop here. Frequently it happens that an extension of the inflammation occurs to the aortic valves. If such an extension takes place the pathogenesis is always the same. There is first the production of an aortic insufficiency which may heal and remain healed indefinitely, or the morbid process may go on to the production of an associated aortic stenosis. "Rheumatic" aortic insufficiency in symptomatology and physical signs is very unlike the description of the aortic insufficiency of the text-books. The reason for this is that up to the present time the aortic insufficiency of the text-books has always been syphilitic aortic insufficiency, whereas there are two varieties of aortic insufficiency almost as different as daylight is from dark—rheumatic and syphilitic. The description of aortic insufficiency should be entirely rewritten from this point of view, and we should no longer speak of abstract aortic insufficiency. We should speak of rheumatic aortic insufficiency on the one hand and of syphilitic aortic insufficiency on the other.

In most cases, therefore, a glance at the individual will lead you shrewdly to infer the probable presence of a rheumatic heart, on the one hand, or of a renal, syphilitic, or arteriosclerotic heart on the other. The age of the individual will go far in leading you to a preliminary determination. The history of the individual will tell you a great deal. If he has a heart which had bothered him in earlier life or for years, or which has interfered with his getting insurance during the third decade of life, it is almost certain that the patient is suffering from a rheumatic heart.

2. **Syphilitic Heart.**—A syphilitic heart, to adopt a Hibernicism, is not a heart at all—it is an aorta. Of course, syphilis does affect the heart, especially in the acute cases, when there is produced a syphilitic myocarditis. Sometimes a syphilitic myocarditis crops up some years after the initial lesion, usually as a dyspnea of sudden, mysterious origin occurring in an adult somewhere around the fortieth year, who has been previously perfectly sound as to his heart. Such a sudden onset of dyspnea

associated with rapid heart action in a man in the forties ought always to raise in the examiner a suspicion of specific origin.

As I have already stated, however, a syphilitic heart, in general, is an aorta. By that I mean to say that when the spirochetes attack the cardiac mechanism they really first attack the arch of the aorta. They seem to have a predilection for the ascending portion, though they often, of course, attack the transverse and descending portions and, indeed, any or all of the arteries of the body.

Syphilis is a great dilator. Its effect is invariably to widen the aortic arch, to produce a weakening of the aortic wall, with subsequent stretching. It is a dilator *par excellence*. The dilatation may be so slight as to justify merely the diagnsosis of a dilated arch, or it may be great enough to merit the diagnosis of aneurysm of the fusiform type. Often it is a matter of taste with the examiner whether he shall designate a case syphilitic aortitis with dilatation, or syphilitic aortitis with aneurysm. There is no hard-and-fast line of demarcation between the two conditions. If the patient lives long enough the dilatation leads to the aneurysm.

When the spirochetes invade the aortic arch they not infrequently invade also the aortic valves, and when they do they always stick to their law of dilatation. Their effect upon the aortic valves is invariably to produce an aortic insufficiency. There is absolutely no such thing as syphilitic aortic stenosis. It is wholly contrary to the law of syphilitic pathology. If you have reason to suspect the existence of aortic stenosis in a case you are examining—if, for example, the criteria of von Leube are present and the pulse is a *pulsus tardus et parvus*—then probably your diagnosis is wrong and the case is rheumatic instead of syphilitic.

Many years ago Adolpf Strümpell called attention to the fact that there was the closest relationship between aortic disease and syphilis. When I first began to study medicine it was asserted that 45 or 50 per cent. of aneurysms were specific in origin. As time has gone on the percentage of syphilitic aneurysms has steadily risen, until now we feel sure that pretty nearly all aneu-

rysms are on a specific basis, comparatively few of them being due to senile arteriosclerosis or other very rare conditions. I remember very well when Strümpel first called attention to the association between tabes and aneurysm in support of his contention that both of these conditions were syphilitic in origin. We know now that such association is extremely common, large numbers of cases being met with in clinics constantly, especially since we have been freely making use of the fluoroscopic method of examination of aortic arches.

There is another interesting phenomenon connected with the syphilitic heart, and that is the very frequent association of angina pectoris with syphilitic aortitis. Great credit should be given to Clifford Allbutt for his early insistence upon the relative frequency of incipient syphilitic aortitic infection in angina pectoris. Now we know that many cases of angina are on a specific basis. It is now the rule for almost all examiners to insist that a Wassermann examination be made in all cases of angina. This rule of practice has been found to be essential because of the frequency with which syphilis has been found associated with angina. If I encounter a case of rather early angina with early signs of precordial pain, or a feeling of substernal compression, I invariably ask for a Wassermann test. To be sure, it frequently is negative when I have every reason to believe it should be positive. This is in accordance with the teaching of Warthin, who, in his work on syphilitic hearts at the University of Michigan, found large numbers showing spirochetes either in the myocardium or aorta in individuals who during life had given negative Wassermann reactions.

In whom do we find the syphilitic heart? We find it in men and in some women in the fourth or fifth decades of life. The story of almost all of them is that they have been well all of their lives as to their heart until comparatively suddenly, within a year or so, an almost complete cardiac breakdown has taken place. That leads us to the history of the individual whom we are going to show this morning, but before taking up his case, which will afford some additional information in regard to syphilitic hearts, we have further to consider the two remaining cardiac groups.

3. **Renal Heart.**—This is the heart of the individual who has reached middle adult life. It is the *cor bovinum*. It is the heart of high blood-pressure. Acute glomerular nephritis does not give rise to the so-called renal heart. The renal heart is the product of chronic interstitial or glomerulo-interstitial nephritis and of high blood-pressure. It is the hypertrophied heart, the heart with a very large left ventricle, the heart with a ringing aortic second sound due to the very high degree of back-pressure in the arteries. It is the heart which occurs in cases of polyuria, in cases in which the urinary output in the night exceeds the urinary output in the day. It is not the heart which shows many murmurs, for in the vast majority of cases none are found until the stage of dilatation from overstrain due to high blood-pressure is reached. It is not a difficult heart to recognize. Inspection of the individual will frequently lead you to judge the case as to type.

4. **Arteriosclerotic Heart.**—The arteriosclerotic heart is the heart of the aged. I do not mean by this that the individual must be aged in the sense that he is old in years, but I do mean that he must be aged in the sense that he is old in his arteries. He is the individual with a marked tortuosity of the temporal arteries, the individual who has begun to lose weight or who is already under weight, the individual with the moving brachial arteries and tortuous radials. Not infrequently his blood-pressure is not especially high. In many instances it may not be much above 130 mm. systolic, but he betrays his arteriosclerosis in other ways. It affects oftentimes his coronary arteries or his brachial arteries, and not infrequently his renal arteries. It affects his whole body, leaving it undernourished, and causing a gradual loss of weight. It is usually a comparatively easy matter in looking at the individual who complains of his heart to tell whether he belongs to this arteriosclerotic type or not. His appearance and age alone carry great weight in the final estimation.

If, then, you are confronted with an individual who is making some complaint as to his heart, the first thing for you to do is not to have him take off his coat and vest and roll up his shirt so you may apply the stethescope, but your first duty rather is

to inspect the individual as a whole, to size him up and make a mental estimate, to ask yourself whether in your opinion he belongs to the rheumatic group, the syphilitic group, the renal group, or the arteriosclerotic group. You will be surprised in the vast majority of cases to see how rapidly you can answer this question. You will find that you can conclude with a high degree of probability by your inspection of the individual as a whole that he belongs in such and such a group. This greatly simplifies the work which you will have to do when you examine his heart. You approach your patient understandingly; you already know before you begin to examine him a good deal about him. You may even be able to make a diagnosis without examining him. For example, suppose you look at a young man or a young woman about thirty-three or thirty-four years of age who is complaining of shortness of breath, and you pick up the hand and feel of the radial pulse and find an arhythmia and inequality, a rapid heart action, and a pulse which is somewhat small—possibly a thready pulse—you will have no difficulty whatever in saying off-hand that the young lady is suffering from a double mitral lesion, so characteristic is the pulse of this condition. On the other hand, if you meet with a man about forty-five years of age whose arteries are throbbing quite a bit, whose radial pulse shows quite a high anacrotic arm, a *pulsus acuminatus* at the top, with a sharp descent of the dicrotic arm, a *pulsus celer et altus*, the water-hammer or Corrigan's pulse, you know at once you are dealing with a syphilitic aortic insufficiency. Such a pulse could not belong to an aortic insufficiency on a rheumatic basis; it could only be a syphilitic aortic insufficiency. You would not get in such a quick diagnostic estimate, for example, all the details of the development of his lesion, but you would have a primary working basis for an attack upon the diagnostic problem, and you could work up the conditions actually present in his case at your leisure.

This is a rather lengthy preliminary statement of the fundamental principles to be had in mind when one approaches a cardiac case, and will make for us the demonstration of the present patient a matter of comparative simplicity.

The patient is a man fifty-seven years of age. He is unmarried and by occupation a waiter in one of the clubs of this city. For several years he has been engaged in this occupation. His habits are those of the class to which he belongs. He has consumed a fair amount of alcohol in his life. He has used all the tobacco that he wished, and although he does not admit having had a specific lesion, still, he is an unmarried man with a history, which he frankly admits, of gonorrhea. He entered the hospital October 16th because he was unable to work any longer.

Let us see how he was before the onset of his present illness. Every year up to this last year he has been able to work without any particular difficulty, but comparatively suddenly he has been taken with shortness of breath and general weakness so great that he has been unable to carry on his occupation as a waiter, and has come to the hospital for assistance. He does not complain of very much in the way of symptomatology except for one thing. He complains that he is bothered with a certain amount of compression in his chest; as he expresses it, "he has not room enough in his chest" or "he feels crowded in his chest." This has been associated also with some definite pain located in the so-called precordial area, although, as a matter of fact, it ought rather be called in his case the supracordial area, since the pain lies rather high instead of at the level of the heart. He does not admit, however, that the pain has extended into his left arm or that it has come down the ulnar nerve territory into his little finger, as so often happens in true angina pectoris. He does notice a fact which many of these patients observe, namely, that the pain bothers him quite a bit at night. He also has observed that exercise makes his shortness of breath much shorter, and that circumstance has compelled him to give up his work and come to the hospital for relief.

On entrance, the night of the 16th of October, his pulse was 92, his temperature 96.4° F., and his respirations 26. He walked into the hospital, but was immediately put to bed on account of the dyspnea which was present, and a back-rest was ordered because of orthopnea. During the day his respiration was very difficult and at night he became so very much distressed that

it was thought advisable to give him ¼ grain of morphin sulphate at 10 P. M. Notwithstanding this, he slept but four hours during the night. He was also put upon the infusion of digitalis, in the hope that his heart might be somewhat strengthened. You will note that the rate was not particularly rapid, the pulse being only 92.

The next morning, on the 17th of October, his pulse had dropped to 84, but his temperature still remained subnormal, being but 97° F. in the forenoon and 96° F. in the afternoon. His respiratory rate dropped very little, being 24 practically all day. He was much distressed during most of this second day, but managed to sleep quite a good deal. That night he was so far improved that it was unnecessary to give him any morphin, and the nurse reported that he had a fair night, although he did not sleep very well.

The urinalysis which was made the day after his entrance showed a specific gravity of 1021, an acid reaction, no albumin, no sugar, no red blood-cells, and an occasional small, narrow, hyaline cast. Two days later a similar analysis showed practically the same findings, except that the hyaline casts were much reduced in number, and by October 22d they had entirely disappeared.

The patient entered in a condition of extreme dyspnea on the afternoon of October 16th, and with rest in bed by the afternoon of the 19th was so fairly comfortable that he was permitted to sit in a chair while the bed was being made, and was also permitted to read. On the following day, the 20th, or the fourth day after he entered the hospital, he was in such good condition that he was taken to the *x*-ray room for fluoroscopic examination. Thus, four days of rest, a small amount of infusion of digitalis and an opiate given but once so improved his condition that he could read, sleep, and eat without very much trouble. On the 18th, the second day after his entrance, he was placed upon iodid of potassium because of the nature of his malady. Examination of the blood, which was ordered immediately upon his entrance because of the general picture which he showed, gave a 4+ Wassermann. A count of the blood showed 8400 white cells,

5,428,000 erythrocytes, and 80 per cent. hemoglobin. This indicates a fairly good blood state.

Very interesting is the observation made in regard to his blood-pressure. Although his heart, as we shall subsequently show, was in a state of distention, he has a systolic blood-pressure of 160. In taking his diastolic pressure the laboratory assistant records that it is greatly decreased, being under 50. The pulse-pressure, therefore, is 110.

You will notice that the individual is a man rather tall and well developed and apparently of the same age as he admits, namely, fifty-seven. You will note that he is rather short of breath, and yet that he is able to appear before the clinic without very much evidence of respiratory or circulatory embarrassment. When we proceed to examine this individual we are struck at once by the fact that the apical pulsation is located in the sixth interspace and that it lies in the nipple line. Such downward and outward dislocation of the apex is almost invariably found in one of three lesions—either in renal, arteriosclerotic, or syphilitic hearts. It is not found in the rheumatic heart. The rheumatic heart is the wide heart, and the apex is usually pushed far out into the fifth interspace. It does not sink into the sixth interspace. So diffuse an apex-beat as you note in his case is always a sign of dilatation, hypertrophy, or a combination of both.

Besides the apex-beat you will also note a very spectacular phenomenon, namely, an excessive pulsation in his carotid arteries. You will notice that they almost jump at you and, indeed, the term "hopping carotids," introduced by the French school, is very apt in describing these arteries. You will also notice when looking at his brachial arteries that they are somewhat tortuous and with each pulsation they snake out straight, and then revert to their former position, thus causing a certain degree of apparently lateral motion. You will also notice in observing his brachial arteries that there is a certain amount of arhythmia. Please note this fact, as it has some bearing on the prognosis, as we shall see later. If you will feel of his pulse as his arm hangs down, you will find that he has the water-hammer

or Corrigan's pulse, or, using the Latin term, he has the *pulsus celer et altus*. If you feel of the pulse with the arm elevated you will find this phenomenon still better exemplified. You will also note that the pulse is unequal as well as somewhat arhythmic.

In this connection please recall his blood-pressure findings. The systolic blood-pressure was 160 mm. of mercury, the diastolic less than 50, and the pulse-pressure 110. Pulse-pressure, in general, is an expression of the extent of throbbing. When the individual has a very low diastolic and very high systolic blood-pressure he always has what he calls "throbbing," namely, a very large discrepancy between the systolic and diastolic pressure, and the arteries even jump when they pulsate. Such throbbing is sometimes so great in aortic insufficiency that the pulse-pressure actually equals the systolic pressure. By that I mean that in many cases of aortic insufficiency the systolic pressure may be 160 and the diastolic 0. Since the pulse-pressure is the difference between diastolic and systolic, the pulse-pressure in some cases of aortic insufficiency may be 160 or even more. Zero diastolic pressure is pathognomonic of aortic insufficiency on a syphilitic basis. It does not occur in rheumatic aortic insufficiency.

Throbbing may also occur in cases of vasomotor paresis or vasomotor excitation. Such throbbing, if you take the blood-pressure at the particular time it occurs, is always found to be due to a marked discrepancy between the diastolic and systolic blood-pressure. In the case of chronic interstitial nephritis with approaching cardiac weakness throbbing frequently occurs. As such a patient gets better you will always notice that the diastolic and systolic begin to approach one another, and when the throbbing ceases you will find that it is because the discrepancy between the systolic and diastolic readings has been greatly lessened. In this man's case the very low diastolic and high systolic reading is extremely suggestive of syphilitic aortic insufficiency. Indeed, one might almost base the diagnosis upon this fact, taking also into consideration the man's general appearance and his brief history.

When you percuss his heart you find that he has a moderate

cor bovinum. The heart is enlarged considerably, extending to the right of the sternum about 1 inch and extending to the left of the nipple line. The dulness is found as low as the sixth interspace and as high as the second. Indeed, the dulness which one finds in the upper part of his chest is such as to raise the presumption of possible enlargement of his aortic arch, either in the sense that he has a dilated aorta or that he has an aneurysm. When you percuss in the second interspace to the right of the sternum you find slight dulness there. Huchard, years ago, called attention to dulness in the second right interspace as a sign of aortitis, and his observation has stood the test of time. Thus far in our examination we have evidence that the pathologic process has reached a high degree of cardiac hypertrophy, perhaps of dilatation, with the usual obvious signs of syphilitic aortic insufficiency.

On listening to his heart we are at once struck with the fact that we are hearing a number of murmurs. When we listen over the apex of the heart we hear a systolic and diastolic murmur. When we listen over the base of the heart in the second interspace to the right of the sternum we also hear a systolic and diastolic murmur. Has this man a rheumatic aortic insufficiency and stenosis and a rheumatic mitral insufficiency and stenosis? In answer to that question we would call attention to the fact that he has always been well until the last few months, and within a comparatively short time he has gone all to pieces as far as his heart is concerned. This is not the story of rheumatic heart disease. We find, on questioning him further, that he has not been the victim of any acute infection which could have as its sequel a rheumatic infection of his heart. It seems, then, altogether unlikely that he has a rheumatic double mitral and rheumatic double aortic lesion. Furthermore, when we listen to the aortic area more carefully we at once discover that von Leube's criteria, which are so important in the diagnosis of aortic stenosis, are not present. It is true that we cannot hear any aortic second sound in his case, but it is equally true that he has no loud, sawing systolic murmur over the second right interspace transmitted up into the right carotid artery, and that he has no

palpable systolic thrill in this location, and, finally, that he has not the characteristic pulse described by Broadbent, the *pulsus tardus et parvus*. Moreover, on feeling of his pulse any one of the gentlemen here would at once say that it would be impossible for a pulse of this character to be present if there were an associated aortic stenosis. His aortic systolic murmur then must be due to another thing. It cannot be due to an aortic narrowing. It must be due to an aortitis. When we fluoroscoped him we found that an aortitis is present to a degree so great that in my opinion we would be justified in making the diagnosis of fusiform aneurysm of the ascending arch.

On further auscultation we note a diastolic murmur, indicating aortic insufficiency. This leads us to another consideration. It used to be taught that an aneurysm, fusiform in type, of the ascending arch dilates the ring of insertion of the aortic semilunars to such an extent that they no longer touch when closed, thus causing a "relative" aortic insufficiency. When I first began to study medicine we were carefully taught that in practically all cases of aortic insufficiency the ascending arch was involved because of a relative dilatation of the ring of insertion of the aortic semilunar flaps. We know now this is not the case. Examination of these valves by the Levaditi staining method shows that they contain spirochetes, and what we used to call "relative aortic insufficiency" is now known to be organic spirochetic involvement of the valves. Consequently, we know that this individual, although he has either a fusiform aneurysm or a dilatation of the ascending portion of the aortic arch, is not suffering from "relative" aortic insufficiency, but from true organic insufficiency.

Remember also what I said a short time ago, namely, that there is no such thing as syphilitic aortic stenosis. It is wholly contrary to the nature of syphilis for an aortic stenosis to develop; and when, in the presence of an obscure case of syphilitic aortic insufficiency, you think you find signs of aortic stenosis because of a systolic murmur, hesitate long before you make the diagnosis. In fact, do not make it, for if you do you will be wrong.

Now let us turn our attention to the mitral area. As I said,

you also hear fairly readily in this locality two murmurs, a systolic and a diastolic. They seem to be, to all intents and purposes, quite excellent evidences of disease of the mitral valve, but if there be disease of the mitral valve, can a diagnosis of syphilitic heart stand? Our answer would be No. If there is disease of the mitral valve present in his case with the presence of true mitral stenosis and insufficiency, then his case is rheumatic and our whole diagnosis falls down.

When we examine carefully into his systolic murmur we find that it is not very well transmitted to the axilla. Furthermore, we find that it is not heard in the back. This is a matter of considerable importance because it means that the murmur is not characteristic of true mitral insufficiency. The murmur is not properly transmitted. Is it not just as reasonable to assume that his apical systolic murmur is due to a relative mitral insufficiency caused by gradually developing weakness of the muscle-fibers of his left ventricle, leading to dilatation of the left ventricle and a failure of approximation on the part of his mitral flaps? It is surely true that such a dilatation, with weakening of the sphincteric action of the auriculoventricular septum makes possible the regurgitation of blood from the left ventricle into the left auricle, producing what is called relative mitral insufficiency, or the relative insufficiency of cardiac dilatation. This, then, is the explanantion of the systolic apical murmur, not transmitted to axilla or back.

How, finally, are we to explain the diastolic murmur which is heard at the apex? If you will note carefully this diastolic murmur you will observe that it is not associated with a loud, rolling, or reduplicated apical first sound. Can it be explained on any other basis than that of mitral stenosis? Yes, it is the so-called Austin Flint murmur. In aortic insufficiency the regurgitating blood-stream, shooting back from the aortic arch beneath the mitral flap into the upper posterior right-hand corner of the left ventricle, buoys up the mitral flap and opposes it to the blood which is passing at the same time from the left auricle into the left ventricle. The opposing of this flap to the downcoming blood-stream brings about an artificial narrowing of the

valve space between the left upper and left lower chamber. It therefore produces eddyings in the blood entering the left ventricle, and such eddyings are heard by us as diastolic murmurs. It is not that we hear the diastolic murmur of the aortic area carried by the blood-stream down into the left ventricle, but we hear at this level a real diastolic murmur undoubtedly produced in the left ventricle by the opposition of the mitral flap buoyed up by the aortic regurgitating blood to the oncoming blood from the left auricle into the left ventricle. That is how an Austin Flint murmur is brought about.

We have found in this individual an excellent example of how easily we may diagnosticate a cardiac case by going at it in the proper manner, whereas had we at once started to listen to all four of his cardiac murmurs, we might probably still be floundering around, wondering whether he is suffering from a double mitral and double aortic lesion or not. We perhaps would have entirely missed the great fundamental diagnosis of cardiac syphilis. Approaching the thing from a fundamental point of view we recognize a probable syphilitic in the individual. We note at once that he belongs not to the rheumatic group, but, by his age, either to the renal or syphilitic. We note by his history that he belongs at once either to the syphilitic or to the renal group, and as soon as we examine his urine we are cognizant of the fact that the case must belong to the syphilitic variety. The early determination of the Wassermann reaction was of distinct advantage, because we could then be positive of the presence of a specific infection. The fluoroscopic examination which was early made was also fortunate because it gave us early and indisputable evidence of aortitis and of a degree of dilatation great enough to warrant the diagnosis of aneurysm. Thus, as far as the diagnosis of this man is concerned, we would say that he is suffering from cardiac syphilis, that he has an aortitis and aneurysm and aortic insufficiency, that although he has four murmurs present, he has but one lesion, that the murmurs are easily, readily, and reasonably explained on the basis of one pathologic process, namely, syphilitic aortic insufficiency.

There remain two points which must be discussed rather

briefly. The first of these is his precordial pain and distress. This is an evidence of aortitis, and if it reaches a degree great enough will probably eventuate into true angina pectoris. It is, however, not likely that he will live long enough for the development of such a state of affairs. Sir Clifford Allbutt, in his book on Arteriosclerosis and Angina Pectoris, calls attention to the fact that the only constant pathologic lesion in all cases of angina pectoris is really an aortitis. The old concept that such an angina is due to coronary sclerosis or, in the event of failure to find it on postmortem examination, to angiospasm of the coronaries, this secondary hypothesis being necessitated by the absence of organic coronary sclerosis, has had to be abandoned. At the present time there seems to be a greater disposition to accept Allbutt's teaching that such anginas are occasioned by aortic disease. In his case, therefore, his precordial tightness is another link in the diagnostic chain. It was noted that in his case pupillary inequality, tracheal tug, an expansile tumor, and asymmetry and asynchrony of the radial pulses was not present. Large numbers of mild degrees of aneurysm occur in which these classical signs of aneurysm are wanting. Indeed, in the great majority of aneurysms at the present time we get our diagnosis from the fluoroscopic examination and the *x*-ray plates. When in the case of a precordial distress and anginoid symptoms our suspicions are still further raised by the presence of an aortic systolic murmur, the fluoroscopic and *x*-ray examination is an imperative necessity.

The second point which needs amplification is the presence in this man's case of arhythmia. What does an arhythmia mean in his case? Can it add anything to our diagnosis by its presence? You will recall what I said in regard to mitral stenosis and the effect of disease of the valve-flaps upon the bundle of His It will occur to you that it is a very simple matter, because of the propinquity of such disease in the mitral valves to the bundle of His, for a physiologic or anatomic disturbance to take place in this bundle. How is it with reference to the aortic arch? Can syphilis of the aortic arch with the production of an aortic insufficiency, aortitis, and aneurysm account for the arhythmia

by extension to the bundle of His? The answer is obviously that it cannot. The arhythmia must be due to some intrinsic disturbance in the heart itself. It has long been taught in textbooks that when in a case of aortic insufficiency arhythmia and inequality of the pulse are noted, there is likelihood of early death. This dictum was based entirely upon experience and was warranted by the event. Now the dictum is based upon better knowledge of cardiac disease. We know now that when such arhythmia develops in syphilitic aortic insufficiency, thanks to the work especially of Warthin for proving the presence of the spirochetes in the heart muscle, myocarditis is almost invariably present. What, then, must we conclude in the case of this patient? This, that in addition to the syphilitic aortic insufficiency, aortitis, and aneurysm, he is also suffering from a myocarditis of spirochetic origin. Will this modify the prognosis in his case? Yes, to a remarkable degree. Our experience in such instances is that these patients have not very long to live. They reach their primary cardiac breakdown; and, unlike the compensated cases in the rheumatic heart, the breakdown is a final breakdown. They may live one year, sometimes two or three, but rarely more than that after a syphilitic cardiac breakdown such as this patient has.

NOTE.—The patient was kept on cardiac and specific medication for quite a time, requiring occasionally, because of difficulty in breathing, doses of codein and occasionally also of morphin sulphate. Toward the end of the year he began showing edema in his lower extremities, which is notoriously a sign of great gravity in cardiac syphilis. It is a sign of great gravity because it means a vastly weakened myocardium. At the same time his respirations gradually became more and more labored, so that we noted on the 31st of December that there was a moderate degree of edema of the lower extremities, that his respiration was labored, and that occasionally he was irrational and tried to get out of bed. He also began complaining of pain, some of the pain being abdominal and extremely suggestive of abdominal aortitis and abdominal angina. During the forepart of January he became more and more irrational, trying to get

out of bed and talking at random and sleeping but very little. On January 8th he seemed much as usual, his pulse being 84 at 6 A. M. and 84 at 3 P. M. On January 9th he suddenly took a turn for the worse at 6 o'clock in the morning, but near the close of the day he was pretty much as usual, his pulse being 90, his temperature 96.8° F., his respirations 20. That evening he began to sink rapidly. His pulse rather suddenly began to be very rapid in action, rising to 130 at 7.30 P. M. and his respirations to 30. At 8 o'clock his pulse was 126 and respirations 26. At 8.30 P. M. his pulse was 80 and his respirations 20. At 8.45 P. M. his pulse had fallen to 76 and he was given a dose of camphorated oil. At 9 P. M. his pulse dropped to 54 and his respirations to 24, when he died. The observations in regard to his pulse are rather characteristic of a failing heart from myocarditis. The heart struggles along toward the end, beating fewer and fewer times per minute, until finally pulsation entirely ceases. His axillary temperature when taken shortly before his death showed a temperature of 97.8° F. There was no pulmonary edema or evidence of coronary embolism or thrombosis, or other disturbance of any definite sort. All that one can say was that he very gradually sank on the evening of the 9th day of January, dying at 9.05 P. M. No postmortem was permitted.

CLINIC OF DR. SOLOMON STROUSE

MICHAEL REESE HOSPITAL

JUVENILE DIABETES IN TWINS. THE KARELL TREATMENT OF EDEMA. THE IMPORTANCE OF DETAILS IN THE TREATMENT OF ANGINA PECTORIS.

JUVENILE DIABETES IN TWINS

THROUGH the courtesy of Dr. Julius Hess I have the privilege of showing you today a rather remarkable instance of diabetes occurring in twins at almost exactly the same time. The history of the two cases from birth is identical. The age of the children is eleven years, both were delivered normally, had an uneventful childhood, both had chicken-pox at the age of five, measles at six, and whooping-cough at eight. In the family history there is no diabetes, but on the mother's side there seem to be some cases of pulmonary tuberculosis.

The children entered the Michael Reese Hospital in January, 1918, and the mother gave the following story: A few weeks previously the little girl complained of irritation of the genitalia and increased thirst. Urine examination made by their physician showed sugar. Now because it had always been true that both children had suffered simultaneously from the same diseases, the mother had the urine of the boy examined, and sugar was found in his specimen also.

Going back a little, we find, on questioning the children, that the boy had several attacks of tonsillitis and had his tonsils removed in 1911. Likewise the boy confessed to being a great eater of potatoes and bread, while the girl does not like potatoes, but never missed an opportunity to eat as much candy, bread and jelly, and rich pastry as she could lay her hands on.

When the children first entered the hospital they were both very healthy looking youngsters, perhaps inclined to adiposity. The physical examination was absolutely negative in both children; the blood and stool examinations showed nothing abnormal.

The urine, however, showed a reducing substance, which Dr. Morse analyzed and proved to be glucose.

I do not propose to go into the question of treatment of these children, as Dr. Hess will probably report the cases later. It is interesting, however, to note that they behaved to dietetic treatment in the same way that one would expect a diabetic child to behave. The carbohydrate intake has varied at different times and there was a corresponding variation in the glucose excreted. One examination of the blood-sugar was made in each child; in both instances the low figure of 0.06 per cent. was found.

It is certainly unusual to find diabetic twins. Many authors have reported diabetic families, but I have seen no instance reported similar to this. That these cases belong probably to the class of true diabetics would seem to be a justifiable conclusion from their reaction to treatment, despite the low blood-sugar. In recent years several investigators (Salomon, Riesman) have attempted to separate out of the group of youthful diabetics a mild type which is not severe or fatal. Unfortunately, this differentiation has not resulted in separating the cases of *true* but *mild* diabetes from those of *renal glycosuria*. Attention, however, has been directed to the fact that there may exist in children perhaps three different types of diabetes:

1. The true—usually fatal—diabetes.

2. A mild type of true diabetes, generally occurring in several members of the same family.

3. Renal glycosuria, which is not true diabetes, but is an anomaly of glucose excretion.

The cases presented here probably belong to either Class 1 or 2, but further study and observation of the clinical course would be necessary before definitely classifying them.

From the standpoint of etiology these patients also offer food for thought. In many of our patients a preceding history of an acute focal infection, usually in the tonsil, has been obtained. It is, therefore, interesting to note that the girl never has complained of sore throat and has perfectly good-looking tonsils, while the boy had his tonsils removed seven years ago. It

will, however, be noted that both children admit being heavy eaters of carbohydrate food, the boy of potatoes and bread, and the girl of glucose in the form of candy, jellies, and pastries. Coupling this fact with the incidence of the disease at the same time in children born at the same time, one might be tempted to speculate as to the etiologic relationship of excessive carbohydrate feeding to juvenile diabetes. In a review which I have recently made of the reported cases of diabetes in the young, many patients, especially the infants and very young children, gave a history of glycosuria following almost immediately after prolonged ingestion of a diet containing an excessive amount of carbohydrates. You may also recall the theory of Weichselbaum, that diabetic children are born with the pancreas congenitally predisposed to the pathologic changes which produce the disease. It is, indeed, quite conceivable that in our cases such a congenital predisposition may have existed, and that the continued insults of excessive carbohydrate feeding finally broke the barrier and damaged the pancreas sufficiently to produce glycosuria.

THE KARELL TREATMENT OF EDEMA

CASE I.—The patient is a dentist, aged sixty-one, married, who came to me in November, 1917, for an examination. He gives the following history: He has always been a healthy man, who worked hard all his life; he has never been an alcoholic, hardly drinking at all, and he absolutely denies any venereal infection. Up to November, 1914, he can recall no illness whatever except a slight backache resulting from trauma. Three years ago he had a "breakdown," and was put to bed and treated for myocarditis. Since that time he has been an invalid and complains of the following group of symptoms: Dyspnea on exertion, cough on lying down, a marked swelling of the abdomen, and a general inability to do things. His abdomen has been tapped at intervals of three weeks.

His family history is negative; there are several healthy children and his wife has had no miscarriages. On examination you will see a florid, healthy looking man. There are no dilated venules on the face, nor does his nose give any signs of acne

rosacea. The sclera are clear, the right pupil is slightly larger than the left, and both react well to light and accommodation. The throat is negative and the teeth are in good condition. A few small lymph-glands are palpable at the back of the neck on the left side; otherwise there are no enlarged glands any other place in the body. The thyroid is not enlarged.

Chest.—The lungs, except for a few coarse, moist râles in both bases posteriorly, are negative. The heart apex is beyond the nipple line and the heart is considerably enlarged both to the right and left of the sternum. The heart sounds are sharp and clear, and everywhere over the cardiac area a rough, systolic murmur is heard. There is no accentuation of the aortic second sound. Over the base of the heart and over the aorta this rough systolic blow is heard quite distinctly. The pulse is regular, of good volume, with a systolic pressure of 115.

Abdomen.—At present you notice many atrophic lines over the skin of the abdomen, which, although full, is soft and not distended. Palpation reveals no tender areas. The edge of the liver is easily palpable 4 cm. below the costal margin. The edge is round, very hard, and apparently nodular. No other abnormality is noted in the abdomen, and at present there is apparently no sign of ascites.

The reflexes are brisk, there is no edema of the ankles, and no scars or tenderness over the long bones. A plain specimen of urine just voided shows a specific gravity of 1021, a trace of albumin, no sugar, and a few granular casts. The blood examination reveals nothing abnormal and the Wassermann test is negative.

Diagnosis.—From the history of this man we are practically forced to make the diagnosis of cirrhosis of the liver. Allow me to recall that for months, up to August 4, 1917, the abdomen was tapped regularly every three weeks and much ascitic fluid removed. It is true that this patient has myocarditis, that he also has a disturbance of his renal function, but it is hardly probable that either myocarditis or nephritis could result in the present condition of the liver and the repeated filling of the abdomen with ascitic fluid. Likewise the occurrence of the

aortitis, which is evident from the physical signs in the heart, would support the presumption that here we had a case of cirrhosis of the liver. Now, despite the negative Wassermann and the negative history of syphilitic infection, the probabilities are, of course, that the cirrhosis of the liver is due to the Spirochæta pallida, especially in view of the complete absence of any alcoholic history.

Treatment.—When this patient came to me he was in a condition such as you see him now. That is, his heart was compensated and there was no ascites, and, as a matter of fact, he had been in such a condition for over three months, although up to August 4th he had to be tapped every three weeks. What happened to cause this remarkable change? The patient had read somewhere about the Karell treatment for edema, and, on his own initiative, without the guidance of a physician, had decided to indulge in this treatment. He followed a strict "cure," and for over a week at a time he took nothing but 28 ounces of milk a day. We will discuss the details of the method later. In this case a really remarkable result ensued. The ascites gradually disappeared, the man lost much weight, his girth became so small that he had to have his trousers retailored, and, on the whole, he felt in much better condition physically than he had for years. After the acute stage of the treatment he followed a strict diet in which the salts and water were both limited, and up to February of this year succeeded in preventing the onset of ascites. About the middle of February, despite a rigid adherence to a milk régime, the ascites had again developed to such an extent that tapping had to be resorted to.

Before discussing the details of the treatment in this case I wish to show you another example in which by means of diet we were able to relieve a patient of general anasarca.

Case II.—This gentleman is seventy years old; a man of exemplary habits all his life; there has been in the past two years or less a gradual development of a tendency to dyspnea on exertion, an irregular pulse, and a dilated heart. In his past history there is nothing of particular importance except an operation about fourteen years ago for a ruptured cecum. At this time

the man was desperately ill and only survived after a most trying and critical time. As stated above, he has always been of exemplary habits, never indulged in alcohol at all, smoked but rarely, and denies venereal infection. All his life he has taken good care of himself, and although engaged in the pursuit of big business he has for years not done any hard physical work, and has almost invariably had a daily period of both physical and mental relaxation. He is the father of three healthy children and his wife has had no miscarriages.

Last winter he was continually under the care of physicians and practically constantly under the influence of digitalis in some form or other. Despite this constant care and attention. in the spring his dyspnea became more marked, and in July there was a beginning edema. Up to this time the patient had not been kept completely in bed, as it had always been felt by his physicians that no considerable harm could result from allowing him a couple of hours of business daily. When I saw him in July, through the courtesy of Dr. Otto Schmidt, the dyspnea was so marked that it was necessary to put the patient to bed.

Physical examination at that time showed our patient sitting up in bed, propped by pillows, with rapid, labored breathing; there was distinct puffiness around the eyes, the face gave a general impression of being bloated, there was no cyanosis. The pupils reacted to light and to accommodation and there was a decided subicteric tinge to the sclera. The tongue was heavily coated, the pharynx was normal, and except for one or two teeth that seemed to be in poor condition there was no dental pathology. No glands were enlarged, the thyroid was normal.

Chest.—The lungs showed a definite impairment of the percussion note in the right upper anteriorly and the right base posteriorly. The percussion note in the left base was also dull and merged into the cardiac dulness. On auscultation the breath sounds at the right upper were rough and expiration was prolonged, while over the bases of both lungs the breath sounds were markedly diminished posteriorly; anteriorly in both bases numerous coarse, moist, and mucous râles were heard.

Heart.—The heart apex could not be made out, but there

was a fluttering impulse in the fifth interspace extending practically from the nipple line to the mid-axilla. Owing to the mergence of the dull note due to fluid in the left pleura with the cardiac dulness it was absolutely impossible to outline the extent of the cardiac dilatation to the left. The cardiac dulness extended 4 cm. to the right of the sternal line. The sounds were weak, fluttering, with a marked arhythmia, and a soft systolic blow was heard at the apex. At the base both sounds were weak, neither one accentuated. There was no murmur over the aorta and no substernal dulness. The pulse was very weak, thready, and perpetually irregular; the blood-pressure was 105 systolic.

Abdomen.—The abdomen was full and distended; the liver was easily palpable at the level of the umbilicus, the edge was firm and quite sharp, and was not tender; the spleen was palpable as a firm, round, splenic tumor (patient's wife said that "the spleen has been present for years"). There was a scar of the previous operation in the right lower rectus region. There was some dulness in both flanks which was movable.

Extremities.—The reflexes were active and there was considerable edema of the ankles and legs beyond the knees.

The blood-picture showed a slight, secondary anemia, the Wassermann was negative. The urine excreted in twenty-four hours amounted to between 450 and 600 c.c. It was of a high specific gravity, 1027 to 1030, highly colored, and usually showed a moderate amount of albumin and varying amounts of casts.

Diagnosis.—The diagnosis in this case is plainly a myocarditis, with a dilated heart and no hypertrophy. Secondary to this condition is a generalized stasis of all organs, including the kidney, and a rather definite water retention. The etiology of the myocarditis is not clear; it probably was a premature senility. That the condition is hardly primarily renal would seem to be shown by the history and the findings at the time of the examination.

Treatment.—At the time the patient was first seen by us we had to treat a case of dilatation of the heart, with a complete cardiac breakdown. Bed rest, attention to the bowels, and daily mild sweat-baths were used. The patient was put on a diet con-

sisting of milk, cereals, toast with saltless butter, and orange-juice. The fluids were always limited and carefully measured and salt was practically excluded from the diet. Digitalis was used in various ways, but for five or six days there was a steady downward course.

At this time it was decided to employ an even more rigid dietary régime. The patient was allowed nothing but 28 ounces of milk, given in doses of 7 ounces each at 8, 12, 4, and 8 o'clock. At 6 o'clock in the morning a small cup of black coffee (3 ounces) was given, but nothing else was allowed to pass his lips except cascara at night. Not a drop of water was allowed.

This régime caused considerable distress to the patient, but was persisted in for four days. At the end of this time there had been no increase in the excretion of urine, but the patient had become gradually weaker, the pulse was of a decidedly poorer quality, and the heart sounds, if anything, even more fluttering than at the beginning of the treatment. Fearing the effects of too prolonged starvation, we then added to the diet toast with saltless butter and cereals. He was given two pieces of toast three times and two portions of cereal, with a little sugar and milk, twice in the course of the next two days. Tincture of digitalis in doses of 15 minims every four hours was also started. At the end of two days of this modified diet the desired effect was noted. The urine excretion increased from 500 to 700 c.c. the first day, 1200 c.c. the second, and even to 2100 c.c. on the third day; the edema disappeared practically entirely, the pulse became stronger, the cardiac dulness gradually but definitely diminished in size. However, and this is important to emphasize, the condition of the patient, on the whole, gradually grew worse. On the morning when the urine excretion had risen to 2100 c.c. a dose of Epsom salts was given and was followed by a rather extensive intestinal hemorrhage. Whether this hemorrhage was due to the effect of too rapid osmosis from an intestine already gorged with blood, or whether it was due to a mesentery thrombosis, or perhaps even had something to do with the previous intestinal operation, we could not say. It lasted for a few days, during which time, as a result of the hemorrhage and the pre-

vious starvation, considerable anemia and a condition of marked asthenia developed. This anemic and asthenic condition persisted for a long time after the hemorrhage ceased, although the condition of the cardiorenal system remained satisfactory throughout. The diet was gradually increased until the patient was getting practically everything in unrestricted amounts with the exception of sodium chlorid and of fluids. It was found very quickly indeed that in this case there was a decided limitation to the amount of water which the patient was able to handle. More than 900 or 1000 c.c. was followed practically immediately by edema and a lessened excretion of urine.

The subsequent course of our patient was a gradual but slow improvement of his general condition, and a return of cardiac function which permitted him to walk one-half to one mile at a stretch without dyspnea or difficulty of any sort. In fact, it was almost impossible to realize that this patient in September, walking around and taking care of his business, was the same man who in July was practically moribund from a dilated heart.

Discussion.—It is not always possible to show patients illustrating as well as these two do the power of properly selected diet. Our first patient, whose abdomen had to be tapped every three weeks on account of ascites, due to cirrhosis of the liver, is able to attend to his affairs for six months without the necessity of resorting to the paracentesis needle. The second patient for almost the same length of time is able to take care of big business affairs and lead a life at least of moderate comfort. It could hardly be expected, with the pathologic conditions existing in these two cases, that any treatment would give permanent results, and it is not surprising that both patients have had relapses, which will be discussed later.

The method of procedure to eliminate the retained fluid in both of these cases was the same. The use of restricted amounts of milk without the aid of medicine accomplished the result. The reasons which prompted employment of the restricted milk diet, which is known as the "Karell cure," are simple and logical. The retention of fluid is associated with retention of salt, and, in our cardiac case at least, was due to mechanical inefficiency

of the heart to pump the water through. Milk, as you well know, is an almost ideal diuretic food. It has definite food value, a limited amount of fluid, and a small amount of salt and protein. In addition, it perhaps has of its own accord a slight diuretic action. The one drawback to milk as an ideal food is that in order to furnish sufficient calories properly to nourish a person too much milk must be used. Therefore, in employing the small amounts of 800 c.c., which we use in the strict Karell method, we must realize that we are not giving the patient sufficient nourishment to maintain his body weight. A tremendous loss of body weight which follows a successful Karell cure is due, of course, in great part to the loss of the retained water. But at least in our second case its effect on the nutrition of the patient was quite noticeable, and recalls to mind the need for consideration of this point when we employ the strict régime.

It seems rather strange that the employment of milk and nothing but milk in the strict way outlined will often bring results which could not be obtained by the more liberal feeding. It is probably true that the preliminary treatment prepared the ground for the milk to get in its work. It is more probable, however, that the element of functional rest to the kidneys enters in any explanation of the efficacy of a restricted milk diet. The functional rest which would be obtained by the milk régime, theoretically at least, would be greater than that offered by the more liberal diet, and perhaps it is just this element which, in certain crucial cases, changes the balance in the right direction.

While these two cases illustrate how wonderfully efficient the Karell régime may be, they also illustrate two other points in its employment. The first of these points has already been discussed, namely, the possibility of producing asthenia, which is as serious as the original disturbance. As a general thing, however, one need not seriously consider this as a danger, because in the extreme case of anasarca anything that promises relief is welcome.

The other point is concerned with the permanency of the results. Neither one of our patients was *cured* by the treatment; yet one would be expecting a tremendous amount of any remedial

agent to effect a cure where so marked pathologic changes were present. Of course, a cure cannot be effected when such marked anatomic changes have already occurred. But the question will arise at once whether the milk régime is of benefit in a possible return of symptoms. This point I can answer in regard to both our cases. The dentist with the cirrhosis of the liver had absolutely no effect from the same method of treatment in February, which had proved so successful in August of the preceding year. The gentleman with the myocarditis, however, still reacts splendidly to milk. In the past two months there has been a constant tendency toward development of edema, as we have never been able to increase the patient's salt or water tolerance. Whenever the edema becomes threatening the patient is placed on milk, 7 ounces every four hours, for four doses a day, with 6 ounces of coffee for one or two days, and generally this has been followed by an increased urination and improvement in his circulation.

These two cases illustrate in a striking manner the benefits to be derived from this method of treatment in cases of cardiac, renal, or hepatic dropsy when other less radical measures have failed. Karell published his original work in 1866; and recently Goodman (Archives of Internal Medicine, 1916, xvii, p. 809) has published the results of his experience with the method in over 100 cases. Some of the points emphasized by Goodman as being necessary to the proper use of milk are well worth repetition, as attention to detail is of prime importance.

Choice of Cases.—The method can be used for a variety of conditions, but is especially of value in edema, whether due to cardiac, renal, or hepatic insufficiency. As a means of reducing obesity it also is valuable. A definite contraindication for the use of the Karell method arises when any symptoms of uremic poisoning are noted. In uremia the essential therapeutic consideration is elimination, and the restriction of fluid necessary to the successful employment of the Karell cure may be decidedly harmful to the uremic patient.

Method of Employment.—For reasons perhaps not entirely understood the method, to be successful, must be adhered to

strictly. Milk, 200 c.c., every four hours—8, 12, 4, and 8 o'clock —may turn the trick, whereas the same amount of milk given more frequently in smaller doses may not produce results. It is, of course, true that many patients with edema, perhaps most patients, will react favorably to a less rigid cure. A diet poor in salt, with restricted fluid but containing other foods than milk, frequently will cause marked diuresis, with the loss of edema; but when the patient does not react to such moderate methods and the Karell is finally employed, it should be used in the detailed method outlined. Absolutely no other fluid can be allowed, and Goodman says that "the purpose of the treatment is immediately defeated if the patient is allowed to drink the milk whenever he pleases."

The **effects of the cure** can be seen often in one or two days, but sometimes not for seven or eight days. In my experience the effect has been seen rather early, perhaps due to the fact that I usually try the modified salt-poor, restricted fluid diet before resorting to the Karell. Usually the effect of any diet in conditions involving renal insufficiency cannot be noted immediately, as can easily be proved by following the curve of chlorid or nitrogen excretion in cases of nephritis. Therefore the preliminary preparation makes the soil fertile, and when finally the milk "cure" is given the reaction will be more rapid than in those patients who have been receiving unlimited amounts of salt and water.

Usually the first effect of the cure is a protest by the patient. But, as we have abundantly learned in treating diabetics, even complete starvation will be borne if the patient's confidence is obtained and the promises offered by the method are carefully explained. The thirst of the first day or two soon disappears, and when diuresis starts the patient feels so much better that he is more than willing to continue to the end. In cardiorenal cases, as the floodgates open and the bloated condition fades away into the outlines of normal anatomy, the heart's action improves, the dyspnea disappears, and the transformation from complete invalidism to more or less complete comfort follows.

But again let me emphasize that the patients in whom the

Karell cure is used are damaged goods, and no method of treatment can restore normal function to a heart whose very muscle-fibers are damaged, or to a kidney or liver already marked by permanent pathologic changes. The diet must be properly balanced even after results are obtained from the Karell cure. Almost all such patients have a distinct and definite tolerance for both sodium chlorid and water, a tolerance which must be respected at all times. Therefore, much care is necessary in the gradual addition of food to the diet, and each patient must be individualized. As a guide to treatment I shall show some diet lists arranged purely schematically:

Breakfast.—Stewed fruit, cereal with sugar and a small amount of cream, toast, saltless butter, cup of cocoa or milk.

Dinner.—Potato (mashed or baked), spinach (or other stewed vegetable), small amount of chicken, fish, or well-broiled beef; junket or custard, toast and saltless butter, cup of milk.

Supper.—Cereal with cream and sugar, one egg, creamed celery (or other stewed vegetable), stewed fruit (or baked apple), toast and butter.

(1) Use no salt in cooking.

(2) Add no salt in eating.

(3) Limit *total* fluid intake; 28 ounces (800 c.c.) to 32 ounces (1000 c.c.) are the limits usually advisable.

(4) Foods (also salt and water) are added according to the reaction of the individual patient.

Before closing this discussion I wish to draw attention to the use of drugs in these conditions. You will have noted that in our two patients no drugs were given during the rigid treatment. The patient with myocarditis had been given digitalis preparations to the point of producing toxic symptoms without any noticeable effect on the circulation. Therefore, during the milk cure all drug therapy was suspended, as experience shows how little good arises from drugs during the stage of congestion. Usually the patients on whom the milk cure is used have already been saturated with digitalis or other diuretic drugs, and, as a general rule, it is wise to discontinue all medication (except purgative pills), at least at the beginning of treatment. Judgment

must be used in following this rule, as surely certain patients require the whipping effect of digitalis.

But temporary cessation of drugs during the milk treatment may be followed in a few days by better use of the same drug. For instance, our patient with myocarditis during a recent breakdown exhibited marked gastric disturbances whenever digitalis in any form was given; but after a few days of milk with complete freedom from drugs he was able to take digipuratum without any gastric upset and with a decided influence on his circulatory system. This increased tolerance to digitalis is, I think, one of the most valuable results of the Karell cure.

THE IMPORTANCE OF DETAILS IN THE TREATMENT OF ANGINA PECTORIS

The two patients whom I am going to show illustrate certain points in the treatment of angina which perhaps are apparent to most of you already. However, it seems worth while emphasizing these little things, especially since in these two patients and in others whom I have seen recently lack of attention to these details resulted in many attacks of angina, while as soon as the patient's attention was drawn to them good health resulted.

The first patient is sixty years old and is, as you see, quite a healthy looking man. About a year and a half ago he began to have typical attacks of precordial pain shooting down his left arm into his finger-tips. Up to that time he had been in very good health, was an active business man, and played golf frequently. As far as he knows, the past history has been uneventful except for an attack of typhoid fever as a young man. The attacks of angina were repeated time and time again, and were especially noticeable after meals or after walking. Climbing stairs, interestingly enough, produced no attacks.

His physicians warned him of the dangers of these attacks and, in fact, told him that at any moment he might fall down dead in the street. Under the best medical attention the attacks grew more frequent, so that finally a few months ago when he

came to see me he was having them during the night and when he arose in the morning.

At the time I saw him in October, 1917, the physical examination showed a man in apparently good condition. The eyes had a somewhat haunted expression, as if there were constant fear present. The teeth and tonsils were completely negative, the previous physicians having delved into these carefully. Thyroid was not enlarged, nor was there any general adenopathy. The lungs were normal; the heart was enlarged to the left, extending 15 cm. from the midsternal line. On palpation the apex was somewhat thudding and a systolic thrill was noticeable, especially at the base of the heart. A loud systolic blow was heard all over the heart, more marked at the base and over the aorta. The pulse was regular, slow, of good volume; and the blood-pressure was 145 systolic. The abdominal examination was negative; all the deep reflexes were exaggerated. The urine showed normal amount excreted in twenty-four hours, specific gravity of 1022, a trace of albumin, and a few hyaline and granular casts. The blood examination, including the Wassermann, was completely negative.

The striking feature of this case as it presented itself to me in October was the alarming frequency and the real severity of the attacks. I felt very decidedly that inasmuch as the patient was having his attacks at night and in the morning, even before he got out of bed, and was not having them particularly after exertion, some element in the etiology of the attacks had been overlooked. I told the patient so, and invited his co-operation in discovering what this element might be. After two weeks of observation and frequent conversations with him and his wife, it occurred to me that most of his attacks were produced by psychic stimuli rather than by physical effort. After reaching this conclusion, further analysis of the man's mental condition revealed a status of which even he himself was not aware. He, as well as his previous physicians, thought he was a very brave man who had no fear; as a matter of fact, fear was the dominant characteristic of his whole attitude toward his illness.

It was not the fear of death which disturbed him, but it was

the fear of the pain produced by the attacks. Coupled with this was an intense but repressed desire not to let his wife know how really frightened he was. He was in a state of continual repression. When he went to bed at night he was harassed by the fear of an actual attack and by the fear that his wife might learn of his feelings, and when he awoke in the morning exactly the same condition of affairs was present. He had also had the bad habit of getting out of bed in a hurry, preparing his toilet, eating breakfast and getting off to his office, two blocks away from his residence, without taking the time for any leisurely loafing.

I took great pains to explain to the patient just how attacks of angina are produced, laying especial emphasis on the fact that in many cases just as severe trouble might result from emotional as from physical disturbances. I told him that I was certain that most of his attacks resulted from the tremendous strain under which he was living, and that unless he changed his mental attitude the attacks would increase in frequency and severity. Rather unconsciously we spoke about the influence of the vagus nerve. In reference to the statement about dying in the street, while in no way attempting to minimize the dangers of the disease, I let the patient feel that a proper readjustment of his emotions, a proper and sane view of his own condition would, in all probability, result in lessened attacks. In addition, I urged him to eat his breakfast and read his paper in bed before getting up in the morning. After dressing I ordered him to sit around the house for fifteen to twenty minutes.

All this may sound commonplace to you, but let me assure you that from the standpoint of the patient the results were, to quote the patient, "miraculous." Almost immediately, thanks perhaps to the physical changes in his morning routine, he began to have fewer attacks; and the confidence which the patient obtained from this was followed by an entire change of point of view on his part. He felt that there was some hope, and that if he followed instructions fully he might get along very well. Also he was able, after a little effort, to discuss the whole matter with his wife, and he went to bed at night no longer with the

fear that he might "wake up and find himself dead." Gradually he had fewer and fewer attacks, and at the present time he can go along for days without a single disturbance. Mind you, he passed through the very severe winter which Chicago had, going almost daily the two blocks to his place of business twice a day. When the wind was high and the thermometer low this, we knew, was a precarious thing to do, and it usually caused some distress. The man, however, insisted on the necessity of his attention to business, and on the very bad days conserved his energy by riding in a taxicab.

The most striking feature about this man's case is, I believe, the emotional upset which certainly caused most of the attacks of angina. You will realize that with a heart such as he has at present, readjustment of a man's psychic attitude will not result in a cure, but it will and it did give the man a comfortable existence. From observing the case very closely I am sure and the patient is sure that it was this readjustment of his mental attitude which has changed his life in such a really remarkable way. In making this statement I do not wish to underemphasize the importance of even the small changes we made in his daily routine, but these we will discuss in connection with our second patient.

CASE II.—This patient likewise illustrates how attention to detail in the treatment of angina may change life from a miserable existence of constant pain and worry to one of at least comparative comfort. The patient is a married woman, sixty-five years old, who for many years has been under treatment for "bad heart." I shall not bother you with details of the history which are of no importance from our present point of view, but shall simply give you the essential features of the case.

Last summer she apparently had reached the height of her misery. When I saw her one day in July she was taking as many as fourteen to twenty nitroglycerin tablets a day, on account of the severe attacks of dyspnea and precordial pain, each of which she thought would be her last. Examination then showed the patient somewhat anemic, with a markedly dilated heart and a loud systolic murmur all over. The pulse was rapid but

regular, and the blood-pressure was 170 systolic. The rest of the examination showed nothing of importance. She could not understand why she was having so many attacks of angina, as she was constantly under medical attention and was a very sensible patient, with a full realization of the severity of her condition, but absolutely without any fear of the consequences. She had been sick so long that she no longer anticipated much more from life than a fair amount of comfort—this she was not getting.

The condition of her heart did not offer much hope for any therapeutic effort, but, much to my surprise on questioning her, I found that despite medical care she was neglecting some of the most essential details which might give her relief. For instance, she had been told to rest after each meal, and this she was doing; but before resting she walked from her dining room to her library, a distance of perhaps 75 feet—and immediately she would have an attack of angina. She was having a particularly hard time at night, although she had been following instructions in taking nitroglycerin before retiring. I found that no one had ever suggested to her the use of a back-rest.

Immediately I insisted on two things: First, that she move her Morris-chair into the dining room and take her rest in a semireclining position as soon as she was through eating, and before she took a step except the one that brought her to her chair. The second change I made was to give her a back-rest at night. In this case, as in the first one, a truly remarkable difference was immediately seen. Two days after, when I saw her, she cried with gratitude at the change in her condition. Her nights were peaceful and she passed the day with only two or three very mild attacks. Now, just as with our first patient, it might seem superfluous to call your attention to such simple things as have been enumerated here; and yet, the results more than justify the effort to treat our patients with angina from the standpoint of the ultimate detail.

I do not wish to discuss in full the treatment of this common condition. You all know what the text-books say, and you all know in how many cases excellent results can be obtained. I think it is decidedly wrong ever to adopt an attitude of hopeless-

ness with angina patients. Of course, it is true that any patient who has had angina may drop dead in the street, but it is likewise true that in some patients this knowledge may do more harm than good. Therefore, every effort should be devoted to studying those little details in the patient's life which he has learned by experience will produce attacks. He will at times need your help in ascertaining just what these things are. We should also learn to know what helps the attack in each individual patient. One of my patients got attacks of angina only on those days on which he went to business on the elevated railroad, but as his attacks did not always immediately follow climbing the stairs, he did not realize that the attacks were produced by the extra exertion. When his attention was called to this, he rode to business in his car, and no longer had attacks of angina. One patient had his attacks only during the winter, and he had them even if he stayed at home. A change of climate during the winter months resulted in complete freedom. One doctor found that while nitroglycerin did not relieve his attacks, atropin sulphate in doses of $\frac{1}{60}$ grain had an immediate effect. Many patients will tell you that even when they eat light meals they have attacks of angina, and you can usually find that the cause of these attacks is one of two things, either the patient exerts himself even slightly after his meal, or he is eating something which produces gas in his stomach and presses on his heart. It is not always easy for you to realize how important these little details are; therefore, the patients themselves frequently fail to find the immediate cause of the attacks. The postprandial rest which is so necessary in almost all cases is frequently indulged in only after some physical exercise, which, although apparently negligible, is enough to cause angina.

In conclusion I wish to emphasize again that I have made no effort to discuss in detail the treatment of angina, but I have merely attempted to bring to your attention the importance of going into details in eliciting the patient's story. By careful observation and individualization much misery can be prevented from entering the lives of these patients, over whom always hangs the shadow of the dark valley.

CLINIC OF DR. CHARLES A. ELLIOTT

WESLEY MEMORIAL HOSPITAL

RADIUM TREATMENT OF LEUKEMIA; ONE CASE WITH SPLENECTOMY

RADIUM in the treatment of leukemia appears to have many advantages over either benzol or the *x*-rays. Benzol has been largely discarded as a method of treatment of leukemia on account of its extremely toxic action, not only on the hemopoietic system but also on the tissues generally, notably the heart muscle. Its action is uncertain and limited and is not followed by the beneficial results noted in either *x*-ray or radium therapy. The reports of the results of *x*-ray treatment for leukemia have been so conflicting that one must conclude that its efficiency depends largely upon the man who applies it. Some roentgenologists report remarkable results and are able to control certain cases for indefinite periods. One patient under observation in this clinic with well-developed splenomedullary leukemia, a woman now eighty-eight years of age, has been apparently well controlled for four years in the hands of a colleague who applied the *x*-ray therapy. This patient continues in good health, the spleen has receded to the rib edge, and the white blood-cells have dropped from 163,200 to between 22,000 and 37,000, but myelocytes are always to be found, averaging from 3 to 11 per cent. The *x*-ray treatment for leukemia leaves much to be desired. Even in the best of hands these controlled cases are still to be recognized as cases of leukemia. The splenic tumor rarely completely disappears and the blood examination always reveals a pathologic condition.

The radium treatment of leukemia offers several advantages over that of the *x*-ray. It is more readily applied, is more decisive in its action, the effects are more lasting, and treatment is necessary only at long intervals.

Technic of Applying Radium in These Cases.—The technic here employed is simple: 100 mg. of radium element in 25 mg. tubes, screened in lead, and raised about ½ inch from the skin by a layer of gauze may be applied with adhesive tape about the circumference of the spleen. The tubes are left in one position from four to six hours, not longer, and at the end of that time they are shifted to a new position about the circumference of the spleen, where they are left for an additional four to six hours. The application of the radium was not continued longer than eight to twelve hours (in two positions of four to six hours each) upon any one day. On the second and third applications, on succeeding days, the tubes are distributed about smaller circles within the circumference, shifting their positions at the end of from four to six hours, as heretofore. The total amount of radium thus applied in three successive days may be 2400 to 3600 mg.-hours. This course of treatment may then be repeated at the end of thirty days, and at the end of sixty days the splenic tumor may be so small that but one such daily treatment of 800 mg.-hours may be made.

In the three patients here presented there have been remarkably good results following radium treatment. After a very few treatments and in a remarkably short period of time the blood-picture has returned to almost normal, the splenic and glandular tumors and liver have receded, and the patients have apparently regained their usual health.

Splenectomy as a cure for myelogenous leukemia was repeatedly resorted to from 1866 (Bryant, Guy's Hospital Reports, 1866, xii, p. 444) to 1890, but with little or no success on account of the great operative difficulties encountered in removing the enormous splenic tumors. A rather careful search of the early literature reveals but one case which is said to have recovered from the operation.

Splenectomy following radium treatment, the spleen being small, may be resorted to without encountering great operative difficulty or undue operative risk, and may be of real benefit in a certain class of cases. The fact that radium applied over the splenic area has such a remarkable result upon the general blood-

picture lends support to the idea that the spleen may play more than a passive rôle in the etiology of splenomedullary leukemia, and the results of its removal after radium treatment will be watched with great interest.

The removal of the spleen in experimental animals causes the white blood count to persist at a slightly higher level than normal, and this effect of splenectomy is to be reckoned with in cases of leukemia treated by splenectomy. The enormous splenic tumor of myelogenous leukemia on account of its size alone is a source of much disability, and splenectomy following radium treatment may be logically resorted to for the elimination of the mass regardless of the beneficial effect splenectomy may have upon the leukemia and without unduly jeopardizing the life of the patient. Such a case is the first here presented.

CASE I. MYELOGENOUS LEUKEMIA WITH RADIUM TREATMENT FOLLOWED BY SPLENECTOMY

Mrs. E. H. O., thirty-five years, housewife, American.

Family History.—Father died at fifty-nine of cancer of the bladder. Mother and two sisters living and well. Husband and three children living and well. No history of tuberculosis in family.

Past Illness.—Measles, scarlet fever, pertussis, varicella, diphtheria when a child. In July, 1914, she was very ill with a supposed stone of the left kidney. Attack subsided without operation. In September, 1916, she was jaundiced, had gastric distress, vomited. Jaundice disappeared without incident after four weeks. Has had frequent attacks of bronchitis.

Present Complaint.—1. Splenic tumor with pain and tenderness in that region.

2. Marked dyspnea and general weakness.
3. Loss of weight 20 pounds from June to September, 1916.
4. Nodules in the subcutaneous tissues.
5. Tingling sensations in arms.
6. Frequent attacks of jaundice with nausea and vomiting.
7. Gastric indigestion, belching, constipation.
8. Frequent urination, especially nocturia.

In June, 1916, patient noticed a mass in the left upper quadrant of the abdomen which was somewhat tender to pressure. This rapidly increased in size until September, 1916, since which time it has remained about the same size, filling the left abdomen and extending to the symphysis pubis. With the increase in the size of the tumor the patient lost weight, strength, and became extremely dyspneic on exertion, and gastric phenomena, such as belching, indigestion, and feeling of fulness after even light meals, developed. Previous to the onset of the present trouble patient had never had headaches, but since June, 1916, she has had frequent and severe headaches, mostly frontal in type, and frequently associated with nausea and vomiting. She dreaded eating on account of distress following. She complains of the heaviness and pressure of the tumor mass. Menstruation was previously normal, but after the onset of the present trouble it has been irregular.

Physical Examination.—Patient is a poorly nourished, emaciated woman of thirty-five years. Skin is rather dark, but no marked areas of pigmentation are present. There are many small tumor masses, apparently leukemic infiltrations of the skin, scattered over the body. Some of these are stated by the patient to be of only forty-eight hours' duration. A number of them are surrounded by hemorrhagic areas. These average the size of a silver dollar. The scleræ show definite icterus and anemia. Tonsils are small. Teeth show several extensive carious teeth, but no evidence of abscesses. Pharynx is granular; otherwise negative. Small glands, split-pea sized, are everywhere just palpable in clusters. Bones show no points of tenderness. Diaphragm is normal, left stands higher than the right, excursion of three fingers. Lungs are resonant throughout, with no abnormal sounds except posteriorly the breath sounds are prolonged over both apices. Capillary circulation is good. The radial pulse is quick and somewhat irregular. The heart area is normal and there is a systolic murmur at the apex, the second pulmonic tone is accentuated; otherwise negative. The abdomen shows a large splenic tumor, the surface is irregular, three distinct notches are palpable at the edge, there is no friction-rub. The liver

appears enlarged, stands from one fingerbreadth below the nipple to the level of the navel, edge is sharp and tender. Surface is smooth except for one area the size of a dollar in the midclavicular line, which extends as a plateau above the level of the rest of the liver. Reflexes are normal throughout, pupils react to light and accommodation. Pelvic examination gives negative findings except for a relaxed perineum, and the uterus appears to be forced into the culdesac by the presence of the splenic tumor. Adnexa are not palpable. The spleen is palpable vaginally.

Blood-pressure is 102 systolic and 64 diastolic; weight 100¾ pounds; urinalysis shows a trace of albumin, no sugar, casts, nor red cells, and an occasional white cell. Blood examination shows 3,648,000 red cells, some poikilocytes, few megalocytes, few microcytes, few normoblasts, megaloblasts, and microblasts being found. White cells 311,200, of which the differential count is as follows: lymphocytes 8 per cent., large mononuclears 10 per cent., polymorphonuclear neutrophils 40 per cent., polymorphonuclear eosinophils 4 per cent., polymorphonuclear basophils 6 per cent., neutrophilic myelocytes 22 per cent., basophilic myelocytes 10 per cent. Hemoglobin 75 per cent. (Dare). She runs an afternoon temperature as high as 100.8° F. Pulse throughout the course averaged above 100. Respiration rate averaged 22.

Upon June 19th, 20th, and 21st, 1917, a total of 2400 mg.-hours of radium element, supplied by the Physician's Radium Institute of Chicago, was applied over the spleen. On the third day the patient had experienced considerable relief from pressure. The spleen was evidently considerably smaller, apparently most of the decrease in size taking place in the anteroposterior diameter, as the mass was much more freely movable. The white blood count dropped from 311,200 to 208,000.

July 13, 1917: After leaving the hospital the patient experienced marked relief, especially in the matter of breathing, and there is now no pain or discomfort after eating. Spleen is definitely smaller. It is more movable and thinner. The hand can be inserted behind the spleen, the abdominal walls being relaxed. There is marked discoloration over the splenic area, but

the skin shows no other evidence of radium burns. The blood-picture has changed, the leukocyte count is less, there are more nucleated reds. There are numerous subcutaneous leukemic nodules on the right thigh and about both knees. There are a few subcutaneous hemorrhages the size of a quarter of a dollar on the left leg.

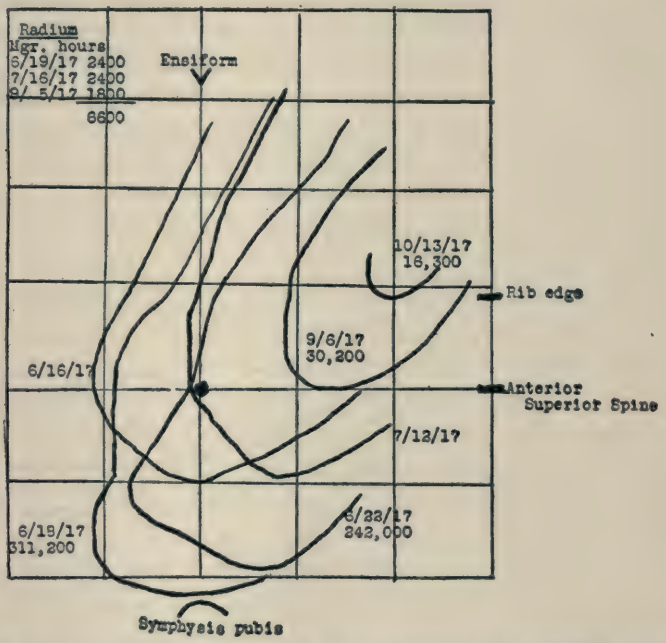

Fig. 211.—Case I. Spleen outlined on abdominal wall according to scale. Note the rapid diminuition in the size of spleen coincident with the reduction in the white blood count following the application of 6600 milligram-hours of radium element.

On July 13th, 14th, and 15th, 1917, the patient again received a total of 2400 mg.-hours of radium element. A total of 4800 mg.-hours so far applied.

July 16, 1917: There has been a decided reduction in the size of the spleen, the liver is still large and tender. Patient sleeps well and feels generally well. White blood count 150,200.

July 21, 1917: Patient woke this morning with a headache,

temperature 103° F., pulse 104, white-cell count 19,000, red cells 3,190,000, hemoglobin 60 per cent. The spleen is much smaller. There is swelling in the right parotid region.

August 4, 1917: Patient has had an acute attack of mumps which was then epidemic in her family, first the right parotid and then the left was involved. She has been extremely ill from this attack. During this time the spleen has become much smaller in size, extending 1 inch below the navel and to the midline. The liver area is still broad, three fingers below the rib edge, and is tender. White cell count 15,950; red cells 3,440,000; hemogobin 69 per cent.; weight 105 pounds. Urine is normal. There are three superficial radium burns over the splenic area.

September 1, 1917: White cell count 19,950; red cells 3,920,000; hemoglobin 67 per cent.; differential count shows lymphocytes 13 per cent., polymorphonuclears 80 per cent., myelocytes 7 per cent. Spleen is much smaller, extends about three finger-breadths below the rib edge, and is 20 cm. from the diaphragm to the tip.

On September 5th, 6th, and 7th, 1917, 100 mg. of radium element were applied over the spleen for three six-hour periods. A total of 6500 mg.-hours have been applied.

October 13, 1917: Weight 128¼ pounds; white cell count 16,300, polymorphonuclear neutrophils 80 per cent., myelocytes 1 per cent., large mononuclears 9 per cent., basophils 2 per cent., occasional nucleated red, hemoglobin 84 per cent.; red cells 3,650,000. Spleen is 2 cm. below the rib edge, 14 cm. from diaphragm to edge of spleen, not tender, firm, movable. One leukemic nodule persists on the left shoulder about the size of a dollar.

November 16, 1917: Weight 134¼ pounds, spleen appears larger, is 15 cm. from the diaphragm to edge. The edge is 4 cm. below the costal arch. White cell count 26,800; red cells 3,820,000; hemoglobin 85 per cent. An alveolar abscess has developed over the upper first molar tooth. Radiographs of this tooth show a large abscess and the tooth was ordered removed.

December 15, 1917: There is a superficial radium burn under the left breast. Patient feels well and in her usual health

otherwise. Weight 139½ pounds, a gain of 39¼ pounds since beginning radium treatment.

December 29, 1917: On account of the apparent tendency of the spleen to enlarge and in view of the uncertainty of the results of treatment, it was decided to remove the spleen, as the immense

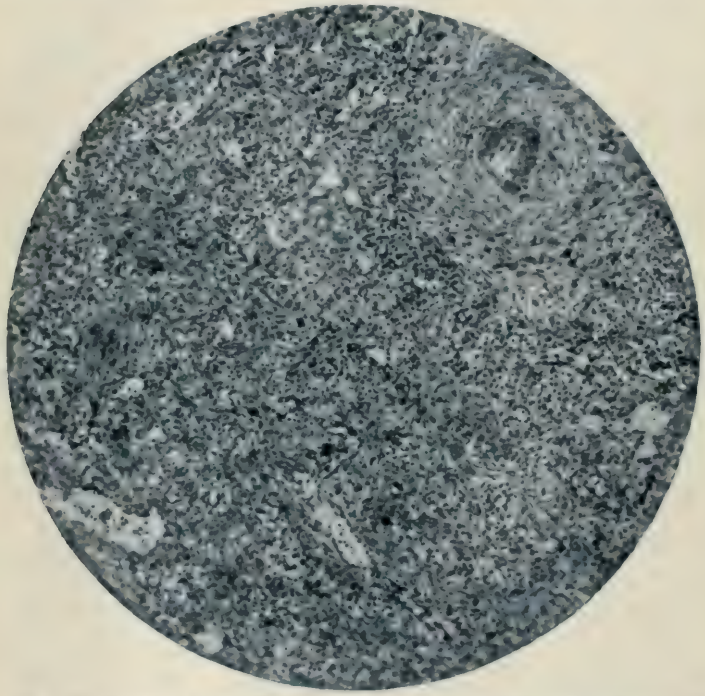

Fig. 212.—Case I. Section of spleen after treatment with radium (6600 milligram-hours). Note diffuse increase of connective tissue. There is considerable deposit of pigment throughout. There is no myelocytic infiltration recognizable as typically seen in myelogenous leukemia. (Magnification 120 diameters.)

tumor mass had been previously a source of great distress. This was done without incident by Dr. H. M. Richter.

At operation the spleen was found to be free from adhesions, the peritoneal reflections were readily peeled off, and the whole spleen was delivered through the incision and removed without difficulty. The vessels were found to be unusually large, the

liver was small, surface smooth, no adhesions. Gall-bladder was filled with small stones. No accessory spleens were found.

Examination of the Spleen.—Weight 300 gm., $11\frac{1}{2}$ x 8 x 4 cm.; firm in consistency; surface is smooth; capsule glistening—not rough. A number of fine yellowish areas can be seen through the capsule. The cut surface is remarkably dry, but not otherwise unusual, no leukemic nodules are apparent.

January 14, 1918: Patient discharged from the hospital in good condition, there having been no untoward effects due to the operation. White cell count 11,700.

February 15, 1918: Weight 136 pounds. Patient feels as well as she ever did. Her only complaint is that of persistent itching at the site of the radium burns, which have healed, but are scaly. The leukemic tumor on the left shoulder persists the same as before. Red cell count 3,870,000; white cells 25,100; hemoglobin 70 per cent.; polymorphonuclears 77 per cent.; large mononuclears 6 per cent.; basophilic myelocytes 1 per cent.; basophilic polymorphonuclears 4 per cent.; lymphocytes 6 per cent.; myelocytes 5 per cent.; Turk irritation lymphocyte 1 per cent.

Comment.—The results of radium treatment in this case are remarkable. What effect the mumps in severe form, contracted during the course of the treatment, had upon the course of the leukemia is a question. The white blood count dropped suddenly at that time. There were no difficulties encountered in removing the spleen. The patient's health at the time of writing (March 14, 1918) is excellent. She has gained $35\frac{3}{4}$ pounds in weight. The blood-picture appears normal, the increased leukocyte count of 25,000 being interpreted normal following splenectomy, reasoning from experimental results on animals. The effect of the radium treatment upon the microscopic appearance of the spleen later removed are such that the tissue would hardly be recognized as that of a leukemic spleen.

CASE II. MYELOGENOUS LEUKEMIA WITH RADIUM TREATMENT

Mr. C. S., forty-six years, carpenter, Danish.

Family History.—Parents lived to advanced age. Five children living and well. Four children died—three stillborn, one in infancy.

Habits.—Drinks occasional beer, moderate user of tobacco, otherwise negative.

Previous Illness.—Typhoid at sixteen, severe course without complications, otherwise always well except for occasional attacks of migraine since childhood.

Present Complaint.—1. Large splenic tumor filling the left abdomen.

2. Dyspnea and general weakness.
3. Loss of weight.
4. Advancing anemia.
5. Polyuria and nocturia.

In the spring of 1915 the patient first noticed dyspnea and advancing weakness, but he continued to work. In July, 1916, he noticed that he had become pale and there was an increase in the dyspnea to such an extent that he could not walk up a flight of stairs. In December he by chance noticed the tumor mass in the left abdomen, and he believes that it has not grown in size nor changed in consistency since first observed. Polyuria has been present for five months; he awakens from three to four times at night to urinate, but has had no other distress. He has never had hemorrhages of any sort, no tenderness over the bones. The loss in weight has been but slight.

He is thin, anemic, no edema or jaundice. He appears to be a well-developed man, tonsils are moderately enlarged, just visible between the pillars. The heart area is 10 cm. in transverse diameter. There is a systolic murmur at the apex and base. Precordial pulsation is prominent. Lungs are negative. The abdomen shows a massive splenic tumor 1 inch to the right of the navel and 1 inch below the level of the anterior superior spines. Surface is smooth, painless. There is no friction-rub to be heard. The liver is enlarged, with the lower border

1 inch below the navel. Abdomen otherwise negative. Reflexes are normal.

On May 25th patient developed an attack of renal calculus with intense pain, vomiting, and on the second day thereafter passed a small renal stone, with relief of symptoms.

Radium was applied irregularly by Dr. Frank Simpson from May 26th to June 30th, a total of 6600 mg.-hours, the amounts

Fig. 213.—Case II. Photograph of case of myelogenous leukemia, May 29, 1917, at beginning of radium treatment. Note emaciation. Spleen occupies whole of left abdomen. White blood count 294,000.

Fig. 214.—Case II. Photograph of same case, March 11, 1918, eight months following last radium treatment. Note absence of cachectic appearance, increase in weight, healed scars of radium burns. Spleen not palpable, white blood count 11,200, no pathologic cells.

and duration of applications varying. During his stay in the hospital there was a marked reduction in the size of the spleen, and upon discharge July 3, 1917, it extended to 1 inch below the navel and 1½ inches to the left of the midline. White cell count was reduced from 294,000 to 33,000. He looks and feels well.

September 5, 1917: Patient's general condition is excellent, the spleen is not palpable. White cell count 6000, no pathologic cells found.

December 18, 1917: White cell count 11,000; red cells 4,010,000; hemoglobin 95 per cent. Patient seems in good health and strength, looks well, and has gained 35 pounds. Spleen is just palpable, extends 1 inch below the edge of the rib on deep inspiration, is not tender. Teeth show some pus pockets, and he was referred to the oral surgeon for treatment.

February 8, 1918: Patient is in good health, feels better than he has for several years. Spleen is not palpable except on deep inspiration. Weight, 164 pounds.

March 11, 1918: Patient is apparently in good health. Spleen is not palpable. The healed scars from radium burns cause no discomfort. Red blood count 5,640,000, no nucleated reds, the stained specimen shows no pathologic cells; white blood count 11,200; differential count: lymphocytes 14 per cent., large mononuclears 3 per cent., polymorphonuclear neutrophils 80 per cent., polymorphonuclear eosinophils 1 per cent., polymorphonuclear basophils 2 per cent., hemoglobin 90 per cent. (Dare).

Comment.—The effect of radium treatment in this case leaves nothing to be desired at this writing (March 14, 1918), eight months following completion of the radium treatment. The patient appears well, has gained in weight, the spleen is not palpable, and the blood count is normal.

CASE III. LYMPHATIC LEUKEMIA WITH RADIUM TREATMENT

Mr. P. D. C., fifty-five years, salesman.

Family History.—Negative.

Previous Illness.—Typhoid at forty, diagnosis in doubt. Herniotomy two years ago.

Present Complaint.—The patient had undergone two courses of treatment (August, 1916, and October, 1916) with benzol together with *x*-ray, for lymphatic leukemia, the exact amounts of benzol and *x*-ray treatments are not known. There was little if any improvement as far as his general condition was concerned,

although the white blood count is reported to have dropped from 264,800 cells, of which 98 per cent. were lymphocytes, to 40,800 cells, of which 94 per cent. were lymphocytes. At that time, he states, he had swelling in the cervical regions, axillæ, and groins. His illness had begun two years before that time, *i. e.*, in 1914. He first noticed swellings in the submaxillary region after a "cold," the symptoms of which were a rhinitis and pain in the head. These symptoms and the swellings disappeared without treatment, and remained apparently absent for about six months. Then the submaxillary swellings reappeared and tumor masses appeared in the cervical regions and groins. Patient felt well at the time of admission and has been apparently so throughout the period in spite of the swellings in the regions mentioned. There has been no other complaint.

Physical Examination.—He is a tall, rather thin, anemic individual, with marked tumor masses protruding from the cervical regions, axillæ, and groins. The spleen is somewhat enlarged and is readily palpable. The liver is apparently somewhat enlarged, the edge being palpable on deep inspiration. Retroperitoneal glandular masses are palpable in the lower abdomen. Cardiovascular conditions are normal, heart tones are normal, no murmurs.

January 11, 1917: Radium treatment begun by Dr. Frank Simpson. The radium was given at irregular intervals and in irregular amounts. White blood count was 113,000. The applications were followed by pain in the region and a definite redness surrounding the tumors.

January 30, 1917: He has had fifteen applications of radium in small amounts applied to the glands, with one application over the spleen. There has been a remarkable solution of the tumors. The masses are very soft, pliable, and painless. There has been some soreness and redness following each treatment. The masses in the axillæ are like soft, mushy bags. Spleen is palpable.

February 6, 1917: Patient has had seventeen applications of radium in varying amounts, there being a total of 6600 mg.-hours. There has been a marked reduction in the size of the tumor masses. White count is now 5400, no pathologic cells.

There have been a number of superficial burns over the sites of the tumor masses, especially in the groin, which heal slowly.

May 23, 1917: Except for the radium burns the patient seems very well. He appears anemic. The spleen is just palpable, extending down 1 inch below edge of ribs on deep inspiration. The abdominal glands can be felt on deep palpation, but they feel soft and mushy, the same as the glands in the neck. Blood-picture would not be recognized as one of leukemia. White cell count 11,000.

Fig. 215.—Case III. Photograph of case of lymphatic leukemia, January 10, 1917, before beginning radium treatment. Note glandular tumors in cervical and axillary regions. White blood count 113,000.

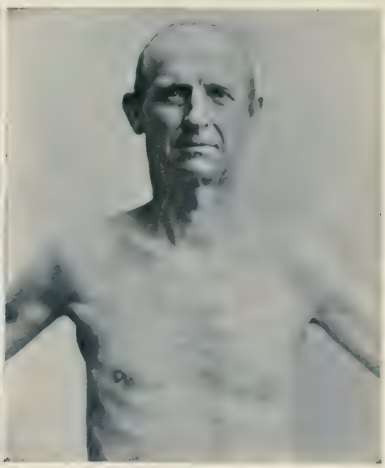

Fig. 216.—February 2, 1917. After three weeks of radium treatment, 6600 milligram-hours in all. Note diminution in size of tumors and improved general condition. White blood count 5400.

This patient left our observation for a visit in California and has not returned. The immediate results of the radium treatment were remarkable for the rapidity with which the masses were reduced in size and the blood count came down to normal. When last seen he was in good health, but we have not heard from him recently, and cannot now speak of the ultimate results of the radium treatment in this case.

General Conclusions.—1. The effect of radium radiation in

the treatment of these 3 cases of leukemia was remarkable, and appeared to be much more effective and certain than other methods of treatment heretofore employed in this clinic.

2. The white blood-cells have rapidly returned to within normal range, and pathologic white cells have largely disappeared from the stained smear.

3. There has been a decided increase in the number of red blood-cells and hemoglobin.

4. The spleen and lymph-glands have rapidly decreased in size, and the microscopic appearance of the one spleen removed following radium treatment shows no leukemic infiltration, as is usually seen in such spleens.

5. The weight, general health, and general well-being of the patients have all improved to a remarkable degree.

CLINIC OF DR. FREDERICK TICE

COOK COUNTY HOSPITAL

EPIDEMIC RESPIRATORY INFECTION

February, 1918.

IT would seem apparent that even the casual observer must have been impressed with the prevalence of respiratory infections during the past few months.

When considered numerically and geographically it would appear justifiable to conclude that some epidemic type of infection is not only frequent but widely distributed. Perhaps the most forcible clinical observation is the extreme bizarre manifestations and clinical course. While a fair proportion begin with symptoms and signs of an ordinary coryza, not a few are initiated with a severe chill, high fever, pains or aches, and other complaints. Physical examination at this time frequently reveals only the findings of an infection of the upper respiratory passage. In some instances, within a few hours or days, the findings develop into a more or less definite clinical picture of some particular type, but frequenty the course and findings remain so obscure that a diagnosis is impossible. During this time not only the patient but the medical attendant must experience much anxiety and perhaps misgivings.

In reviewing the cases under observation, many of them presented in this clinic during the past year, it is easily possible to divide them into two groups:

1. Including those where the infection occurred as a primary clinical entity, followed subsequently by recognizable findings or complications.

2. Those in which the infection accompanied or followed some previous infection, resulting in a recurrence or variation of the previously existing disease.

Before considering these groups in detail it will be of service to indicate the bacteriologic findings as revealed in some of the investigations in the present epidemic.

Most investigators have found a mixed type of infection, including chiefly the influenza bacillus, streptococcus, pneumococcus, Micrococcus catarrhalis, and less frequently other organisms.

With the general unanimity of findings as to the mixed type of infection, there exists a most divergent opinion as to the predominant and exciting organism, and what relation, if any, it bears to the present epidemic. Perhaps this difference of opinion may be accounted for on the variability of the type of infection or organism as observed in different localities under varying conditions.

According to some of the published reports the chief offender is a streptococcus; others have found some type of the pneumococcus, while others would incriminate the influenza bacillus.

Brief reference may be made to some of these findings. Moody, Mathers, and others have investigated the epidemic of respiratory infections in this locality. Moody, by throat cultures on blood-agar in 31 cases, found the Streptococcus viridans, pneumococcus, and a hemolytic streptococcus present in all cases. In only 2 was the influenza bacillus present. Mathers investigated 24 cases by similar methods. The Streptococcus viridans and pneumococcus were present in all; a hemolytic streptococcus in 17, and failed in all to obtain the influenza bacillus.

Williams and Burdick, in Denver, report finding a hemolytic streptococcus and succeeded only twice in over 500 sputum examinations to grow the influenza bacillus.

Ceconi, in the Boston Health Department, considers the influenza bacillus as the chief and determining organism in the recent epidemic. Many similar reports might be cited.

The two organisms most frequently found are the streptococcus and pneumococcus. Serious doubt exists as to the

etiologic significance of the influenza bacillus. Apparently it pays but a minor rôle in the present epidemic.

Clinically considered, the group of primary infections presents many points of interest and not a few problems. As in previous epidemics, pulmonary and cardiac involvement have predominated, but apparently no part of the body is immune.

Infection of the upper respiratory tract is the general rule, with a gradual descending course. Laryngitis, bronchitis, and a bronchopneumonia are frequent, while myocardial or endocardial involvement are by no means infrequent. Accessory sinus infection, otitis media, and mastoiditis have received their proportion, which may also be said of arthritis, renal and neuromuscular manifestations. Meningeal involvement has been relatively frequent. During the past week 2 such cases went to autopsy, with the anatomic findings of streptococcal cerebrospinal meningitis.

Some of the pulmonary disturbances deserve special mention. Particularly frequent and certainly persistent and annoying is a type of bronchial asthma. Following the usual manifestations a subacute or chronic bronchitis develops into attacks of typical bronchial asthma in individuals previously free from such disturbance. The frequency of such occurrence is such that it is impossible to consider it merely as a coincidence, but forces the conclusion of a definite etiologic relationship. These cases therapeutically are hardly short of exasperating.

Instead of the manifestations assuming an asthmatic type, the infection persists and simulates a pulmonary tuberculosis. In not a few there is a cough, perhaps paroxysmal, with blood-tinged sputum, slight afternoon temperature, loss in weight and strength, with night-sweats. These symptoms combined with the physical signs of a bronchitis must arouse the suspicion of a pulmonary tuberculosis and may tax to the extreme the differential diagnostic resources. Continued, repeated, and persistent clinical observation over some period of time may finally succeed in at least an accurate clinical conclusion. Along with the bronchopneumonias is to be mentioned lobar pneumonia, and especially the atypical forms as regards physical findings and lung

location, as well as the evident marked tendency to lung abscess, gangrene, and empyema.

Lung abscess and gangrene have occurred with surprising frequency. The marked tendency to asthmatic manifestations, and in others to develop lung abscess or gangrene, has been so evident as to constitute a rather striking feature of the infection. During the past few months 7 cases of lung abscess, 2 associated with empyema, have been observed. Evidently there is a common basis or cause for the bronchial and pulmonary complications, either some peculiarity of the type of infection or the resulting tissue changes produced by the infection.

As in the previous epidemics, in some of the cases the chief complaints have been abdominal. Not only gastro-intestinal but quite circumscribed and limited to some particular region, suggestive of pelvic, appendical, or peritoneal involvement. A limited number have presented a clinical picture with either splenic or hepatic findings. In three instances the spleen was enormously enlarged, with slight enlargement of the liver and with a secondary anemia.

In one of the cases a splenectomy was done and a hemolytic streptococcus isolated from the spleen tissue. The remaining two refused operation or even blood transfusion; one of which terminated in recovery, the other was fatal. Autopsy could not be obtained.

One instance of hepatic involvement is under observation and will be presented.

Present History.—Female, age thirty years, entered the hospital December 16th with the following history: Seven weeks ago she had a severe cold and sore throat which persisted for about one week. Six weeks ago, one week after the onset, she had abdominal pain and cramps, followed by nausea and vomiting, which recurred during a period of about one week. During this time a marked lumbar stiffness and lameness developed. Then followed a week of improvement, with a second attack of nausea, vomiting and pain, which continued only a few days.

One week ago she had sharp pain in the hepatic region. Pain was severe, increased by moving, deep breathing, and cough-

ing. No nausea, vomiting, or jaundice was present. During the past four days she has been confined to bed on account of the pain in the right side and cramps in the abdomen. With the exception of the usual diseases of childhood she has always been well.

Physical Findings.—Examination revealed the signs of an enlarged, tender liver without jaundice. Hepatic dulness anteriorly extended upward to the third rib, posteriorly to lower angle of the scapula. Lower border of the liver, in the nipple line, was midway between the costal arch and umbilicus. The liver surface and border was smooth but very tender, especially in the gall-bladder region. The splenic dulness increased, but palpation was questionable, owing to tenderness. Traube's space was practically absent. No ascites or distended veins were present. The apex of the heart was in the fourth space and in the nipple line; no murmurs present. During the first two weeks in the hospital temperature in the morning was normal; in the afternoon it would reach 101° or 102° F. Pulse was between 108 and 116, with respirations 22 to 28 per minute. The temperature during the third week was practically normal, at the end of which it again increased, reaching 101° F. in the afternoon for four days, since which time it has been normal. Remaining physical findings were normal.

Laboratory Findings.—Blood examination: Hg., 88 per cent.; reds, 5,420,000; whites, 17,600 on admission and 15,400 one week later. The blood Wassermann was negative. The urinalysis was negative except for slight albuminuria. Repeated gastric and stool examinations were also negative.

x-Ray Report.—Screen findings: Right costophrenic angle cloudy, left costophrenic angle clear. Both apices light up well. Plate: The right diaphragm is unusually high, such as is seen in subphrenic conditions, such as abscess, large liver, etc.

Exploratory puncture in the postaxillary line, eighth and ninth interspaces, was negative.

A clinical diagnosis of an acute infective hepatitis, and possible cholecystitis, was made after excluding, so far as possible, thoracic, subdiaphragmatic, and other hepatic or abdominal disease associated with the symptoms and signs as presented.

Treatment consisted of an antiseptic gargle and internally acetyl salicylic acid (gr. x) t. i. d. during the period of pyrexia.

At the present time she is free from symptoms, the liver has gradually decreased in size to practically normal.

Previous or accompanying disease with associated epidemic infection has constituted a fair proportion of the cases. This is particularly true of the recurring chronic bronchitis and asthma in which acute exacerbations or attacks follow the infection.

Two other pulmonary diseases, tuberculosis and pneumonia, apparently are much influenced by this complicating infection. It would appear reasonable, in the presence of an epidemic, to assign to it the definite atypical course as observed in these diseases. It is even possible that many of the recently detected cases of pulmonary tuberculosis are due to the activating influence of the secondary infection. Many such cases might be cited. In one at least the respiratory infection was promptly followed by an acute pulmonary miliary tuberculosis in an individual of fifty-four years of age whose previous health had always been perfect. Not only the irregular and atypical forms of pneumonia but also the high mortality may be due to the same cause.

The findings in a recent clinical study will be of interest in this connection. During the four-month period from December 1, 1915, to April 1, 1916, there were 501 cases of lobar pneumonia admitted to this hospital, of which 201 died, or a mortality of 40 per cent. In conclusion:

1. Until further bacteriologic investigation it will be impossible to assign any one specific organism as the microbic cause of the recent and still existing epidemic.

2. The preponderance of evidence is definitely opposed to the influenza bacillus as an active factor.

3. If it be admitted that influenza, or la grippe, is due to a specific organism, the bacillus of Pfeiffer, it will be impossible to designate the present epidemic by such terms. It will be necessary to employ such terms as "epidemic respiratory infection" or, perhaps better, to limit the names now in common use—grippe and la grippe—to the mixed type of infection to the exclusion of the specific bacillus.

4. The relative frequency of asthma, pulmonary abscess with cavity formation, and irregular types of pneumonia with complications suggests some definite common pathologic cause. Until further investigation the work of Jobling and Peterson is not only worthy of serious consideration, but may be accepted as a working basis.

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CLINIC OF DR. CHARLES SPENCER WILLIAMSON

COOK COUNTY HOSPITAL

PRESENTATION OF A CASE OF POLYCYTHEMIA—VAQUEZ'S DISEASE

THE case today is a patient in whom I am very much interrested. Before he came into the hospital I was called in consultation on the case, and when he came into the hospital he happened to be placed on my service. He came here for some *x*-ray treatments. He is a man of intelligence, a painter by trade, native of America. He entered the hospital with the examining-room diagnosis of "myelogenous leukemia." His trouble had been diagnosed previously as pernicious anemia, but neither of these is correct. He came in complaining of three things: First, a swelling in the left side of the abdomen; second, weakness; third, shortness of breath, coupled with pain on the left side of the abdomen.

Onset and Course.—He commenced to have pain a year ago in the upper part of the left side of the abdomen. The abdomen was increasing in size. The pain was dull in character, as a rule, but was sometimes sharp, and was made worse by walking or trying to work. He had these attacks of pain, but paid no attention to them until about eight weeks ago, when they became much worse and he went to a private hospital. At this time he was told that he had a large spleen which should be treated. He then went to another hospital for *x*-ray treatments. He had six of these, the last a week ago. These treatments were superficial because they did not have an apparatus adequate for deep treatments. None of the symptoms which he presents at present bear any relation to the *x*-ray treatments.

He worked up to eight weeks ago. He thinks the tumor in the left side has grown larger within the last eight weeks. The

weakness was gradual in onset; it was not very marked until three or four months ago, but since that time has been very marked. Shortness of breath has been present for many months, steadily getting worse. He thinks he has lost about 10 pounds in weight in the last two months. The only other thing that he complains of is that he is subject to frequent sore throat.

Family History.—The patient is single; his father and mother are dead, cause unknown. He has one brother and two sisters living and well. There is no history of carcinoma or tuberculosis, and no history of any condition similar to this.

Previous Illnesses.—Has had frequent attacks of tonsillitis and something which was diagnosed as "grip" three years ago. He denies venereal diseases of all sorts.

Habits.—He has taken no alcohol in the last year, smokes and chews moderately. His appetite is good. Bowels regular, urination normal.

Examination.—As we look at the patient we see that he is rather thin, sparely built, with long fingers, and we are at once struck by the peculiar color. It is a little difficult to define, but when we look at the face we see that it is rather a curious shade of bluish red. The lips are distinctly cyanotic, the ears are bluish red, the arms the color of raw beef. In striking contrast to this is the hand, which is rather pallid, with just a tinge of red color about it; the finger-nails, however, show a moderate degree of cyanosis, although not of very high grade. The prominence of the cheeks and the top of the nose show this color very well marked. On the neck we see curious mottlings. The lower extremities show about the same findings.

The Head.—The scalp is negative; the ears and nose are negative except for the color. The pupils are equal, regular, react promptly to light and accommodation. Examination of the mouth shows the teeth to be in only fair condition. Inasmush as he has been a painter we have examined carefully for lead intoxication, but no lead-line can be seen. The tongue is somewhat coated on the dorsum. On the under surface is a very dark, cyanotic color which is quite striking. There is a little elevation on the dorsum of the tongue, which is a scar, the

result of an accident when he was a child. The rest of the mucous membranes are perhaps a trifle darker than normal, but not markedly so. The neck shows no rigidity and no abnormal pulsations of any kind.

The Chest.—It is poorly developed, rather emaciated, expansion is fair and equal on both sides.

The Lungs.—The borders are normal; they move with perfect freedom. There is no impaired resonance and no râles are present.

The Heart.—The apex-beat is not to be felt accurately, but there is a pulsation of diffuse nature which seems to be the apex-beat, closer to the median line than usual and behind the sixth rib. The absolute flatness is at the lower margin of the fifth rib, extends two fingers to the left of the middle line and to the middle line on the right. The relative dulness is a fingerbreadth to the right of the sternum, three fingers to the left of the sternum and the lower edge of the third rib. The heart sounds are clear. There is no accentuation of either the aortic or pulmonic tone and no murmurs are present.

The Abdomen.—Inspection reveals a brownish discoloration on the left side of the abdomen due to a superficial *x*-ray burn. The next thing which strikes us is that the left upper quadrant is very protuberant, and that he has a couple of very large veins running down to Poupart's ligament, and then up to the upper part of the chest into the axilla. As we palpate the abdomen we find that except in the left upper quadrant it is not protuberant. The abdominal walls are quite rigid, although there is no particular tenderness. On palpation the most striking thing is the tumor mass which extends down to about a fingerbreadth below the navel; it comes over to just a fingerbreadth to the left of the middle line. You can feel the edge very distinctly. It is sharp and rounded, the surface is smooth, and he complains of a little tenderness when I press upon it, but I think this is due to the tenderness of the skin over it. The tumor lies right up under the ribs. It is very superficial, moves deeply with inspiration, and one can feel two well-marked notches on this edge. It is not worth while to go into the subject of what this tumor is because it is so manifestly a great big spleen. On palpating further we find in the

right upper quadrant a mass which comes down just below the navel and which I can grasp between my hands in the front and back. It feels like the right kidney, somewhat larger than normal, not tender. In addition to this I can feel the liver quite distinctly coming down about two fingers below the edge of the ribs in the nipple line, and in the median line it comes down to about two fingers above the navel. The surface is smooth—no irregularities at all. The lung-liver dulness anteriorly is at the lower edge of the sixth rib in the nipple line. I can feel nothing else abnormal in the abdomen.

In the groin there are two or three enlarged inguinal glands on each side, perhaps the size of small beans. In the axilla I can feel two or three glands about the size of peas. The epitrochlears I cannot palpate. There is no evidence of any free fluid in the abdominal cavity. The genitalia are entirely negative and the extremities show nothing abnormal except changes in the color of the skin, already referred to. The reflexes are all perfectly normal.

DR. WILLIAMSON: What is the matter with him? What is your diagnosis?

VISITOR: There must be something wrong with the circulation or with the blood.

DR. WILLIAMSON: The blood-pressure is 142 systolic, diastolic not noted. On the 19th, when he entered the hospital, the blood showed 13,120,000 reds, 35,000 whites, and the hemoglobin percentage was 135 (Sahli). The next day the red count showed 13,280,000. On the 22d, 13,544,000; on the 23d a little under 15,000,000 reds were present. This erythrocyte count is, I need hardly say, a most extraordinary one, and, to make sure of its correctness, I have repeated the count with the Buerker apparatus, which is by far the most accurate for enumerating the red cells. The count made by this apparatus gave just a shade under 15,000,000 reds. The coagulation time was taken with the Wright coagulometer, and the time was less than one minute. The fragility test was made, the hemolysis being complete in tubes 2, 3, and 4, but very trifling hemolysis in tube 5. The differential count showed 93 per cent. polymorphonuclear neutrophils, 1 per cent. large mononuclears, 2 per cent. small mononuclears, 3 per

cent. polymorphonuclear eosinophils. In a smear the reds looked quite normal or as if containing a little less hemoglobin than normal. There was no poikilocytosis. To be sure that the hemoglobin would be taken accurately, and because the ordinary hemoglobinometers are very inaccurate, I took the blood and examined it spectrophotometrically. It contains just 22 grams of hemoglobin per 100 c.c. of blood.

You will see from the charts, which are taken from an article by me in the Archives of Internal Medicine, that this is nearly as high a concentration as the normal infant has at birth. It is not very generally known that there is a great variation in the amount of hemoglobin at various periods of life, and that there is no such thing as a normal percentage of hemoglobin for all ages alike. While this was known as far back as Leichtenstern's day, the idea has not penetrated very deeply into the minds of most physicians, and we still hear of men, who should know better, taking the hemoglobin of, say, a mother and a year old child on the same instrument, making no allowance for the age variation. Now that, of course, leads to the treatment of many children for "anemia" who are, so far as their blood is concerned, quite normal.

I have, in the article mentioned, examined the blood of over 900 normal individuals spectrophotometrically, and, as you will see by an inspection of the chart, which summarizes the findings, the hemoglobin age curve is a very definite one. Now for this patient's age, between thirty and forty, the normal hemoglobin value is about 17 grams per 100 c.c. In our patient the hemoglobin is 22 grams per 100 c.c. Reducing this to percentage, we find that it is about 129 per cent. Now the erythrocytes varied between 13,000,000 and 15,000,000. Assuming 14,000,000 as the average, and calling the normal 5,500,000, we find the percentage of corpuscles to be 254. This is interesting, since it shows that while there is a considerable increase in the hemoglobin, this increase lags far behind the increase in the corpuscles in the ratio of 129 to 254, the color-index being just over one-half its normal value. It is plain, then, that whatever be the underlying pathology of this disease, in this case at least it effects an increase in the

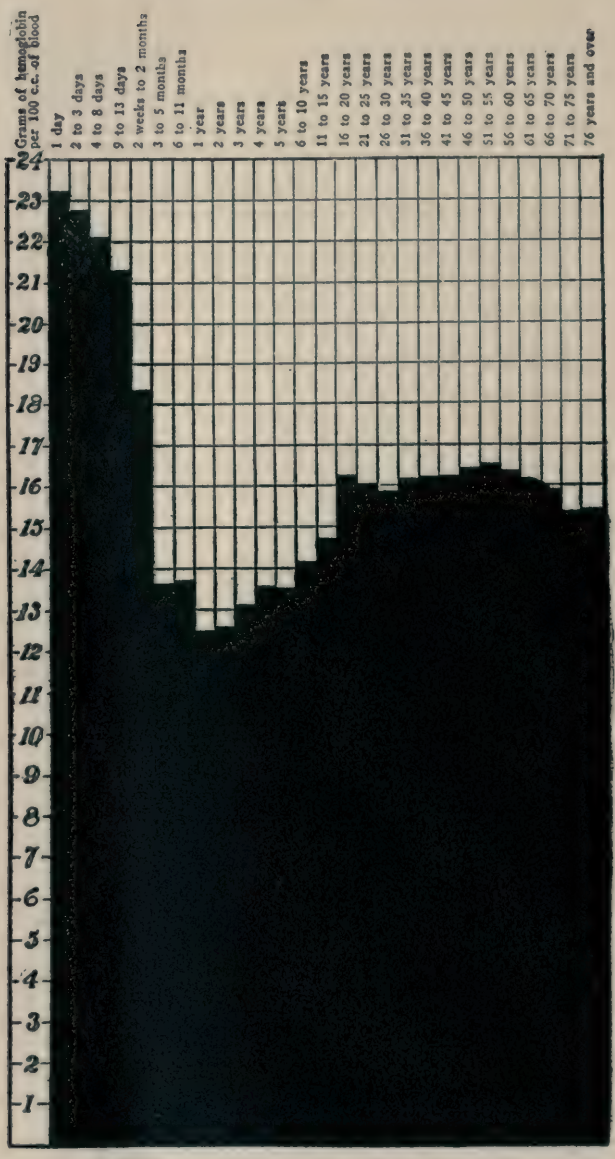

Fig. 217.—Grams hemoglobin per 100 c.c. of blood in persons ranging in age from one day to over seventy-six years.

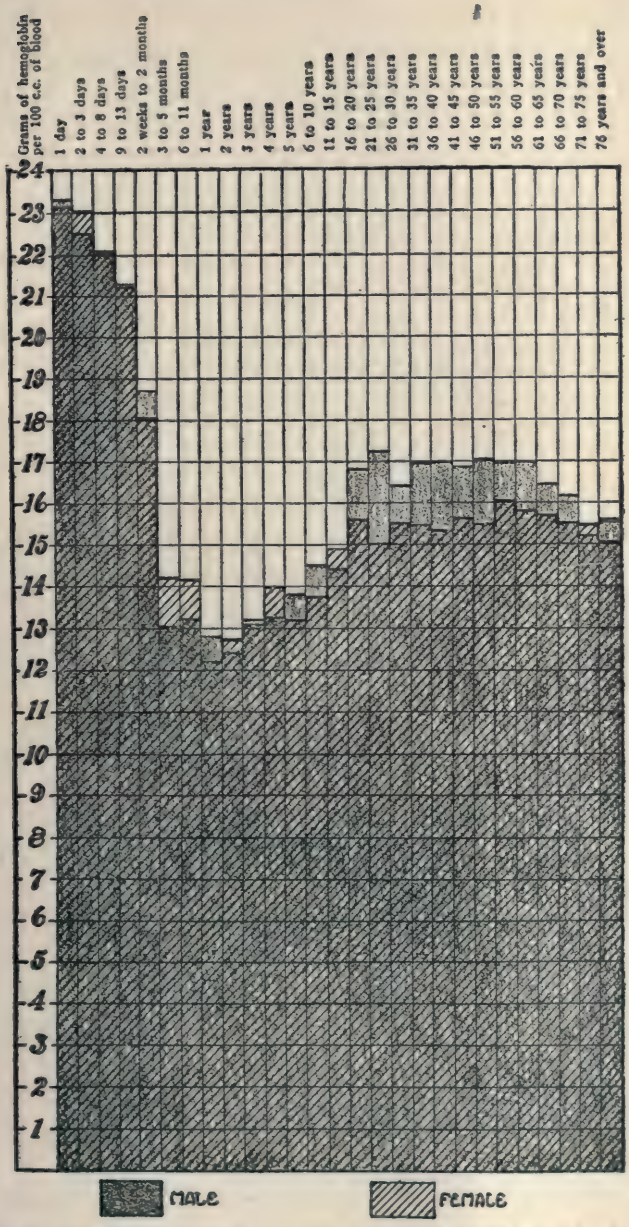

Fig. 218.—Grams hemoglobin per 100 c.c. of blood in the male and in the female, for the ages ranging from one day to over seventy-six years.

erythrocytes far beyond that of the hemoglobin, so that the impression we obtained by looking at the blood-film that the reds are a little paler than normal is amply justified (Figs. 217, 218).

The urine is clear, specific gravity 1020, amber color, acid reaction, a trace of albumin, no sugar. A centrifuged specimen shows an occasional hyaline and granular cast and one or two red cells. The feces showed nothing abnormal.

Now has anyone a suggestion to offer as to what is the matter with him?

When we analyze this case what are the salient points? The first thing is the enormous number of red cells. The second thing is the greatly enlarged spleen, and the third thing is the peculiar cyanosis. We classify the conditions in which there is an increase in the red cells in very much the same way as we classify the condition in which there is an increase of the white cells. In the case of the white cells we speak of leukocytosis and in some cases of leukemia. In the cases with increased red cells we speak of polycythemia. There are two groups of conditions in which we get the increased number of red cells. The first is the symptomatic polycythemias and the second is the primary condition, where there is no other disease that we can find. The secondary erythrocytoses are especially the congenital heart diseases. In these diseases we find every now and then increase in the red cells—7,000,000, 8,000,000, or even 9,000,000. This is sometimes temporary, and sometimes at autopsy we find changes in the bone-marrow. The normal yellow marrow of the bone becomes red. That is probaby the commonest case. Then there are increases in the red cells in conditions associated with cyanosis. We had a case recently with a much higher degree of cyanosis than this, but it was a purely mechanical cyanosis. They are usually temporary and do not represent a real increase in the cells, but merely an altered distribution. If the skin is greatly congested it simply means that there are more red cells in the skin than normal, and this may disappear if the cause clears up. Sometimes in mitral lesions we find this condition, but when the circulation improves the abnormal distribution tends to disappear. There is a peculiar type of intestinal disturbance

in which we find a peculiar type of cyanosis. Then we have a well-marked cyanosis in certain cases of chronic poisoning with certain coal-tar products. I have, within a year or two, treated a woman of great social prominence, whose cyanosis was becoming steadily greater. In her case it was due to liberal doses of a well-known proprietary drug containing acetanilid in large amounts. There is in these cases, however, no increase in the red corpuscles, so that they are readily distinguishable from the cyanosis of a polycythemia.

This patient has none of these conditions. His heart and lungs are normal. I very carefully demonstrated to you that there is nothing like a valvular condition, either acquired or congenital. In contrast with this we have the condition known as primary polycythemia, or erythremia—Vaquez's disease. Vaquez described this disease about 1899 or 1900, although he was not the first to report a case of it. Rendu and Widal had reported a case before. Osler also reported a series of cases. It is a rare disease. Up to 1906 there were about 50 recorded cases. Since then a number more have been reported, but I doubt if there are many over 100 cases in the literature now that are genuine instances.

I will give you a short sketch of this disease and then we will compare it with this case. The principal thing about it is the great increase in the number of red cells. This increase is constant, not dependent upon distribution. We find it in blood taken from a vein or from a finger. There is a constant high level. The second thing about the disease is the peculiar color. The face is a brick-red color when warm and intensely cyanotic when it is cold. The cyanosis varies a great deal; sometmes it is high grade and sometimes not. The third characteristic is the enlargement of the spleen in most cases. You see the findings are very typical. We have hundreds of conditions in which we have a diminished number of red cells, but the cases in which there is an increased number are very limited. The combination of increased red cells, the enlarged spleen, and the chronic cyanosis is an absolutely unique picture and practically pathognomonic.

This is a disease of adult life. The majority of cases have

occurred between thirty-five and sixty years of age. Two or three of the early cases showed a tuberculosis of the spleen, but it was afterward proved that the tuberculosis had nothing to do wth it because in some instances nothing was found in the spleen. As a rule, the spleen is only moderately enlarged—not the enormous enlargement found in leukemia.

As I said, the cyanosis varies greatly. I saw a case in Vienna in 1898 or 1899, before the disease was known. The patient was a woman with a big spleen and she was as blue as indigo. The case was studied and an autopsy obtained, but nothing came of it. It was not described at that time, but it undoubtedly was a very pronounced case of Vaquez's disease.

The Blood Features.—The principal feature is the erythremia —9,000,000 or 10,000,000 is an average case. The hemoglobin percentage is low as compared with the corpuscles. The patient may have 125 or 135 per cent. hemoglobin, so each corpuscle is not as rich in hemoglobin as the normal.

As to the white corpuscles, there is nearly always a moderate leukocytosis, and this is generally due to an increase in the polymorphonuclear neutrophils; occasionally there are a few basophils found, and occasionally a myelocyte. The blood is dark purple red and extremely viscid. The viscidity of the blood is enormously increased and that is of diagnostic importance. It clots very readily.

As a rule, we do not find any changes in the heart. One would suppose that with such a viscid blood it would produce a hypertrophy of the left ventricle, but ordinarily it does not.

These are the principal points of the disease. The etiology is almost unknown. So far as the morbid anatomy is known we know that most cases have shown that the yellow bone-marrow has been converted into red bone-marrow. The relation of the spleen has not been very well established, but most cases show some enlargement of the spleen. It is customary to divide the cases, but it is probably better to classify them all as erythremia or polycythemia.

Another interesting feature is that the total volume of the blood is increased; it is a real plethora. That has been deter-

mined in many ways. In this case, also, we attempted to determine the total volume of blood by the determination of the hemoglobin, spectrophotometrically, before and after a copious intravenous injection. Owing to the very rapid clotting our attempt was not successful. We shall attempt it again at the first opportunity.

The course and duration of this disease is chronic and it extends over a number of years. In most cases there are marked remissions; the patients get better and worse, but the great majority of cases die after a greater or lesser interval of time. The prognosis is, in most instances, fatal. As you see, it is a disease which presents very striking features. We might ask ourselves whether there is any other condition in the spleen which could present this picture, and we would have to say "No." Tuberculosis, syphilis, endothelioma, and Gaucher's disease do not. It is a peculiar disease and the etiology is at present unknown.

The cardinal diagnostic points are these: A patient with (1) a moderately high-grade erythremia, (2) with a moderate increase in the whites—the increase being principally in the polymorphonuclear neutrophils, (3) with an enlarged spleen, and (4) with or without a high blood-pressure. With these present there is practically no chance of going wrong. You must rule out all conditions due to intoxications, to other diseases of the spleen, and all heart diseases. The majority of cases of congenital heart disease do not live to adult life, but this must nevertheless be considered.

The **treatment** of cases of this sort is thankless. The one thing that should not be done is to remove the spleen. That hastens the fatal issue. The best results have been said to be obtained by *x*-ray treatment, and that is what we are using in this case. I am decidedly skeptical as to its value. Frequent bleedings have been advocated, and we shall probably do that in this case also.

As I said before, the cases are extremely rare. I was shown a very mild case two months ago in another city, but one usually goes for a great many years without seeing a case.

CLINIC OF DR. M. MILTON PORTIS

COOK COUNTY HOSPITAL

LESIONS OF THE RIGHT UPPER QUADRANT OF THE ABDOMEN. DIFFERENTIAL DIAGNOSIS

You have had presented to you 8 cases showing different types of lesions of the right upper quadrant of the abdomen. In most of these the diagnosis was definitely made because of the clinical, laboratory, and *x*-ray evidence which you have just gone over. I purposely selected typical cases so that you could make the diagnosis more clearly. However, most of the cases that will come to you for such a diagnosis will not be so definite, and it will be your problem to consider atypical signs and findings in weighing the points for or against a diagnosis.

From the outset I wish to make clear that the more my experience increases, the more am I less inclined to accept a diagnosis of a functional disturbance of the stomach. The terms "hyperchlorhydria," "hypersecretion," "nervous cardialgia," and a host of others, all of which signify neuroses or functional stomach troubles, and are accepted by many as a diagnosis, I am growing more convinced are merely a cloak for our ignorance. Evidence of the operating room as well as autopsies shows a large part of these cases to be sufferers from organic disease. The percentage of functional cases will always be with us, but it will grow decidely smaller as our knowledge increases.

The differential diagnosis of lesions of the right upper quadrant of the abdomen in the typical cases is very easy. In the atypical cases, especially those associated with complications, the diagnosis is not only extremely difficult, but at times impossible. Before giving the differential points I shall, for the sake of clear-

ness, give the important signs and symptoms of these lesions, especially those which are of importance in the differential diagnosis.

The *peptic ulcer* of the stomach occurs more commonly in women, in young adult life. Some cases are latent in their picture, while many present symptoms of hyperchlorhydria with pain from time to time. The onset is insidious, at first with a feeling of fulness and distress, and then later pain, nausea, and vomiting.

Pain is the most important of the symptoms, and the time of its appearance helps to distinguish gastric from duodenal ulcer. Generally it appears a few minutes after eating, but may be delayed to an hour. It is made worse by food, especially coarse food, and increased by epigastric pressure. If vomiting occurs, pain is relieved. The pain is of a burning or gnawing character and not cramp-like. When the pain is continuous, then some complication is present, and we no longer have a simple gastric ulcer. Sometimes the pain is referred around to the back and there is also tenderness in the region of the tenth dorsal vertebra, especially to the left of the spine. Boas attaches a diagnostic importance to this tenderness and has devised an algesimeter to measure it. A localized epigastric tenderness is usually present.

In all of the cases hemorrhage occurs sooner or later, and it is a complication. In most of the cases the blood can only be detected by chemical or microscopic methods in the stomach contents or the stools. In many, however, it is a visible hemorrhage. According to the amount of blood lost, the effect on the patient and the appearance of the patient will vary, and the blood, if large in amount, will be bright in color, and dark if small in amount, especially if it has remained for any length of time in the gastro-intestinal tract. *Usually* death does not occur from hemorrhage from a gastric ulcer.

Vomiting does not occur in *all* gastric ulcers, but it is common, and when it does occur it is usually at the height of digestion, *i. e.*, two or three hours after eating.

The examination of the stomach contents in 95 per cent. of the uncomplicated cases shows a hyperchlorhydria in which the

free acid and the total acid may be two or three times the normal. Occult blood is usually present and macroscopic blood is common.

The motility test in uncomplicated ulcer shows a premature emptying of the stomach.

Duodenal ulcer is more common in males from twenty to forty. Patients at first complain of a general discomfort and sense of weight. Later they complain of pain two or three hours after eating. When liquids are taken, pain comes earlier. The pain is relieved by taking food. Moynihan describes the pain as a "hunger-pain," and says it often wakes the patient in the early morning. This is relieved immediately by taking food or alkalies, and the patient goes back to sleep.

There is at times tenderness in the epigastrium a little to the right over an area 2 or 3 inches in diameter. The upper part of the right rectus muscle may show some rigidity.

Many cases exhibit a *periodicity* to attacks and complete abeyance between attacks. These may follow exposure to cold or wet, indiscretion in diet, or mental shock or worry. Again, the attack may be cut short by rest or by a vacation. *Chronicity* is a common story, and cases may extend over as many as forty years, with periods of intermission.

When a stage of obstruction due to contraction of an ulcer scar or adhesions occurs, then we get a characteristic picture of motor insufficiency. Peristaltic waves are visible on the external surface from left to right, and inflation shows the presence of the large stomach.

Hemorrhage is a complication, and is a *late symptom*, for it usually means erosion of a deep vessel. The ulcer should be recognized before this stage. Occult blood is present in every case, and will always be found if sought for repeatedly.

The *stomach test* in *recent* duodenal ulcer usually shows a hyperchlorhydria just as in gastric ulcer. In the *chronic cases*, however, the titrations may show subacidity. The motor power is very good if no mechanical obstruction is present, and the stomach may even empty too quickly.

In the differential diagnosis of gastric from duodenal ulcer

the time of the pain is very important. If it appears early, within an hour, it speaks for a gastric ulcer, while after two hours it means a duodenal ulcer.

The recurrence in seasons occurs in duodenal cases.

Vomiting is more common in gastric ulcer and rare in uncomplicated duodenal ulcer.

Gastric syphilis may so closely simulate ulcer and cancer that it must always be considered in the diagnosis. Evidence of syphilis in other parts of the body, a positive Wassermann with the blood or spinal fluid, *x*-ray evidence which does not fit carcinoma and has some characteristic things in favor of lues, improvement under treatment—all are definite factors in deciding the diagnosis. If the case should be operated upon and tissue removed in which spirochetes are demonstrated then only can you have a positive diagnosis.

Disease of the gall-bladder in typical cases is easy of recognition, but in atypical cases the symptoms are anomalous, and difficulties of diagnosis arise which are almost insurmountable.

The presence of jaundice with a gall-stone attack makes the diagnosis easy. However, many patients never have jaundice. Likewise, the finding of gall-stones in the stools determines the diagnosis—but in most cases no stones are passed. Gall-stones are more common in women, especially middle aged. A history of a previous attack of typhoid is important.

The *pain* in gall-stone colic is excruciating—much more so than ulcer unless the ulcer is in the perforating stage. The pain occurs independently of eating, is not relieved by food, and may even be made worse by it. The pain is felt in the right upper abdominal region and is often referred to the right shoulder-blade. It appears within an hour of food taking, *especially after greasy foods*.

Chilliness or even a chill may accompany a biliary colic and fever may be present. Vomiting occurs soon after the initial pain, and often with sweating and depression. Nausea and vomiting occur in gall-stones without colic, leading the patient to believe that the trouble is with the stomach.

Tenderness over the gall-bladder is common, and one may palpate tenderness of the liver in the region of the gall-bladder or find a Riedel lobe that is tender.

The *stomach test* shows a normal stomach-picture with normal motor power unless there are complications present such as common duct stone or adhesions causing mechanical obstruction; often a subacidity is found and rarely a hyperchlorhydria.

Perforation of a gastric or duodenal ulcer will produce a similar picture to a severe gall-stone colic.

In perforation there is an acute, violent, tearing, constant pain, followed by collapse, rigidity, tympanites, and loss of liver dulness. A *leukocytosis* occurs quickly, and soon the picture of generalized peritonitis begins, or if subacute perforation has occurred, a circumscribed abscess and extensive adhesions to other organs may result.

Cholecystitis, with or without gall-stones, may simulate ulcer. A pyogenic infection of the biliary passages is usually associated with chills and fever and a leukocytosis. Besides localized tenderness over the gall-bladder area, there are frequently the signs of cholangitis. The absence of the laboratory and clinical findings of the other lesions mentioned is a great help in the differential diagnosis. With adhesions between the gall-bladder and pylorus, motor insufficiency of the stomach may be present. In the interval between attacks of cholecystitis, tenderness can often be elicited over the gall-bladder, especially on deep palpation.

Cancer of the stomach, especially of the pylorus, may cause difficulty, for it frequently occurs on an ulcer basis. The cases with metastatic growths are easy of diagnosis, but before metastasis occurs one can still make the diagnosis by the history and by the palpation of a tumor mass, cachexia and anemia, and the laboratory findings for carcinoma, especially the absence of free hydrochloric acid, and the presence of the Boas-Oppler bacilli along with lactic acid. Numerous biologic tests have recently been developed for the early diagnosis of carcinoma, such as the Salomon test for albumin in the fasting stomach contents, the tryptophan test, the Abderhalden test, and the

complement-fixation test of von Dungern. Although all of these are helpful, none are infallible.

The attacks of *gastric crises* in locomotor ataxia have often been misleading in the diagnosis of these lesions. Many cases, I am sorry to say, have been operated upon with a mistaken diagnosis of gall-stones or ulcer. If a careful physical examination is made such mistakes can be avoided.

The *colic* which occurs in *lead-poisoning* may also be confusing, but here again a careful history and physical examination will avoid mistakes. The referred pain in *appendicitis* or the pain of an abnormally high appendix may give the picture of pain in the upper abdomen, with nausea and vomiting. These cases are all the more confusing because an appendicitis is not infrequently associated with a gall-bladder disease or a duodenal ulcer. The *Dietl crisis* of a floating kidney may give a confusing abdominal picture, but here again the history of an intermittent discharge of a large amount of urine with an improvement of the clinical condition following it, as well as a careful abdominal examination, and, if necessary, a catheterization of the ureters, will make the diagnosis certain. The sudden pain associated with *renal calculus*, *renal new growth*, or a *renal infection* may be confusing, but here again the careful physical examination and a study of the urine with or without ureteral catheterization will help to clear up the diagnosis. Permit me to emphasize to the uninitiated that an examination by all methods, including the *x*-ray, must cover both kidneys, both ureters, and bladder if mistakes are to be avoided, no matter which side is seemingly *the cause* of symptoms. *The rupture of an extra-uterine pregnancy* or an *ovarian cyst* may also give a confusing picture, but this can be eliminated by a pelvic examination. The *colic associated with the passage of some indigestible matter through the bowel* or the acute gastro-enteritis following an indiscretion in diet must also be considered.

Diseases of the *pancreas* and *tumors* of the pancreas are very confusing in the diagnosis of lesions of this region. The diagnosis must largely be made by exclusion. One should never forget the picture of acute pancreatitis with a severe colic, nausea,

vomiting, and collapse, which resembles very closely the picture of perforating ulcer or the rupture of the gall-bladder or the appendix. A localization of the tenderness to the epigastrium, along with a circumscribed distention in this region, and particulary the picture of shock and collapse out of proportion to the other findings, should help make one alert for acute pancreatic disease.

Tumors of the pancreas are troublesome in diagnosis, particularly tumors of benign origin. Malignant tumors of the pancreas are most frequently at the head of the pancreas, and very rapidly produce obstruction of the biliary tracts, jaundice comes on, usually the gall-bladder is palpable, and the laboratory tests are negative for the stomach and bowel. The *x*-ray is negative for disease of the stomach and bowel, but there is frequently *x*-ray evidence of widening of the duodenum as it follows around the head of the pancreas, which is enlarged. The final diagnosis, however, in disease of the pancreas will depend largely upon exclusion of other organs. Stool study for the presence of gas deserves mention, but stool studies are not as satisfactory as the text-books would lead us to believe. You will arrive at your diagnosis by excluding other things.

An *acute intussusception* should be considered very carefully, for it will give a very confusing picture, but the abdominal examination will show, if it is high up, a rather flat abdomen, and if the obstruction is low down, a markedly distended abdomen. Nausea, and vomiting which soon becomes fecal, and *x*-ray evidence which is definite, showing the place of obstruction, all are helpful factors.

I have not attempted to consider infrequent or rare lesions which may cause symptoms or signs in the region considered, for this would necessitate a clinic of unusual length. A diaphragmatic pleurisy, pneumonia of the lower right lobe, subdiaphragmatic abscess, splenic anemia, and syphilis of the liver may give rise to findings in the upper abdominal quadrant. The definite physical, laboratory, and *x*-ray findings of these lesions will help to eliminate them in the differential diagnosis. The last named, syphilis of the liver, deserves special mention,

for the clinical picture is so variable and the history often impossible to determine. The picture of gall-stones may be simulated very closely by syphilis of the liver, and it is well, whenever the slightest doubt that a liver pathology is present, to have a Wassermann test made.

In a previous issue of the MEDICAL CLINICS OF NORTH AMERICA (Boston Number, January, 1918) Dr. Arial W. George, Dr. Ralph D. Leonard, and Dr. Frederick W. O'Brien have a splendid article on the *x*-ray diagnosis of diseases of the upper right quadrant, and I will refer you to that clinic for information concerning the *x*-ray findings in these lesions. I can heartily endorse the statements made by these gentlemen, and wish to emphasize that the *x*-ray must always be taken into consideration in making the diagnosis, along with the clinical and laboratory evidence which I have submitted to you today.

CLINIC OF DR. ARTHUR R. ELLIOTT

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SYPHILIS OF THE AORTA

We have every reason to believe, both from pathologic study and from practical clinical experience, that the vascular lesions of syphilis constitute the most important changes that are observed in that disease. The endarteritis of syphilis is responsible not only for most serious disintegrating effects upon the circulatory organs but also for many nutritional defects in the organs and tissues generally, this factor being especially important in syphilis of the nervous system. One effect of the renewed interest in syphilis which has been one of the most notable features of clinical pathology during recent years has been a revaluation of the pathologic processes which we associate with that disease. In consequence of this, certain processes occurring late in syphilis, and formerly regarded as nutritive secondaries rather than direct infectious processes, have been taken out of their ancient separate classification as parasyphilis, and placed where they really belong, in the list of true syphilitic inflammatory lesions. Among these none is more important than syphilitic arterial disease and its consequences—aneurysm, aortic regurgitation, angina pectoris. The arterial disease of syphilis is a distinct type, differing from non-specific arterial disease in several essentials, chiefly its mode of development, its usually focal distribution and the general absence of regressive metamorphosis, especially calcification. Microscopically, the endarteritis of syphilis is differentiated from the non-syphilitic variety by the fact that the primary seat of the change is in the media and adventitia along the course of the vasa vasorum, any thickening of the intima that comes to pass being secondary in production. Conversely, in non-syphilitic

types of aortic disease the histologic change begins in the intima and predominates there. The true type of syphilitic involvement consequently occurs only in arteries that are supplied with vasa nutritia. This is why it is so often found in the brain because in the cerebral circuit even small arteries possess vasa vasora, whereas vessels of similar caliber in the extremities not being so provided escape these specific changes. For the same reason we find the ascending portion of the aorta to be usually the primary seat of change in syphilitic aortitis, in contrast to ordinary arteriosclerosis, wherein the changes are briefly situated in the descending aorta. The primary and particular process at work is a chronic indurative, inflammatory involvement of the tunica media of the aorta due to infection by the spirochete. No matter what the end-product may become—dilatation, aneurysm, or valve defect—the lesion is an aortitis. Perhaps in no organ or location of the body is the lesion observed so generally syphilitic as in the aorta. It is true that inflammatory involvement of the aorta has been described as resulting from other infections, but so far as clinical appreciation is concerned they are of small consequence as compared with syphilis. Aortitis may, of course, result from acute rheumatic arthritis and from streptococcus infections generally, and less frequently perhaps may follow other severe acute infections. When the aorta is involved in rheumatism or other acute infections, however, this usually occurs in association with endocarditis and manifests the tendency common to all acute infective secondaries to undergo spontaneous subsidence as the primary cause subsides. Syphilitic aortitis, on the contrary, is a progressive lesion until checked by appropriate therapy directed against the syphilis itself, and manifests even to a greater degree than is apparent elsewhere the peculiar obstinacy which characterizes syphilitic foci. From the frequency with which syphilitic aortitis is encountered accidently at autopsy, according to the statistics of Eich in 42 per cent. of cases, we may assume that the infection of syphilis is harbored in that part of the vascular system for years without detection; indeed, it might even appear that the aorta is one of the most frequent stations in which the infection may obscurely lurk in latent syphilis. From the

practical clinical standpoint accumulating evidence is forcing the conclusion that a persistently positive Wassermann reaction in a patient without evidence of syphilis in the skin, mucous membranes, or nervous system points to the aorta as the next most probable seat of the disease. Larkin and Levy examined the aorta in 19 cases which showed positive Wassermann tests during their course: 17 of these 19 aortas gave evidence of aortitis; 11 of the 19 patients (60 per cent.) died from aortitis and its consequences. Citron used the Wassermann test in all chronic cases of aortic regurgitation, finding it positive in 60 per cent.; Collins and Sachs' percentage in a similar investigation being 84. Warthin, in his very interesting investigations, finds active lesions of the aorta in every case of latent syphilis examined. Bearing in mind this frequency of aortitis in latent lues, it is well that we should consider the possibility of a syphilitic etiology in any case of cardiovascular degeneration of obscure origin. In the majority of cases syphilitic aortitis is a very chronic process having a long latency. Many years may elapse between infection and death with anatomic confirmation of aortitis. About 30 per cent. of all syphilitic patients with clinical aortitis are found to have developed aneurysm, and about an equal percentage sclerosis and retraction of the aortic valve. Before either one of these mechanical defects results the disease is usually latent. After they appear, progress is rapid, often bringing life to an end within two or three years. Early in the course of aortic syphilis involvement of a limited portion of the artery may appear of slight immediate significance, but with its further development may ensue dilatation, aneurysm, angina pectoris, or, most commonly, aortic regurgitation. To detect this insidious lesion before it has advanced to the production of mechanical secondaries is of the greatest importance, clinical recognition enabling us in its earlier stages to forestall the development of these defects by active antisyphilitic treatment. The diagnosis is often extremely difficult, since limited and circumscribed changes in the ascending portion of the aorta without involvement of the valve ring are seldom accompanied by clearly defined symptoms or signs. The greatest difficulty is encountered in individuals not recognized as syphilitic. It is

often the case for aortitis to be the only manifestation of the disease in otherwise latent syphilis, and one may expect in a considerable percentage of cases to encounter a completely negative history of syphilis. The majority of patients coming under clinical recognition for aortic syphilis are in middle life, and experienced clinicians understand the significance of angina pectoris and aortic regurgitation originating in the adult.

The foregoing considerations briefly outlined indicate to you the main points of clinical interest involved in syphilis of the aorta. In this region of the body we observe the full brunt of the disease so far as it effects the arterial system. That the aortic tunic is, of all tissues of the body, the most frequently involved in syphilis is a growing belief. When involved by the localization of the spirochete a chronic inflammatory degeneration is started which may in time result in the most complete disintegration at the very center of the circulation. Aortitis is not unlike nervous forms of syphilis in its long latency and the obscurity of its earlier clinical manifestations, but differs widely from them by virtue of the fact that mechanical factors at work in the aorta abridge the later stages of the disease, hurrying along the termination, when they become operative. That so many cases of syphilitic aortitis escape detection until they have reached the stage of dilatation, aneurysm, or valve defect is a reproach to our methods of diagnosis and shows our lack of appreciation of this common manifestation. A better appreciation of the incidence of nervous syphilis exists, so that examination of the reflexes and of the cerebrospinal fluid is becoming a routine in the examination of the syphilitic. On the other hand, unless the blood-pressure is found elevated or a murmur exists, or the patient has some painful or disturbing symptom referable to the heart, the clinical examination does not comprehend a special investigation of the heart and aorta in the syphilitic. This is neglect, since modern methods of x-ray study of the aorta and heart, carried out in a routine manner, would enable us to detect the existence of most cases of syphilitic aortitis before they had advanced to the stage of serious degeneration. It is to illustrate the capabilities of this method in diagnosis of aortic disease that I shall present a num-

ber of cases, selecting them with the idea of demonstrating the disease in its various stages.

One of the most notable features of syphilis of the aorta is its point of election. It is the suprasigmoid portion of the aortic arch that is the seat of localization in early stages of involvement, from whence it spreads in both directions, threatening, on the one hand, the integrity of the coronaries and aortic valves, and on the other extending until it has involved perhaps the entire extent of the arch. Although primarily a small celled or granulomatous infiltration of the middle and outer coats of the vessel, secondary changes sooner or later become established and may be extensive. These are characteristic not by calcification, as in senile ateriosclerosis, but by gradual corrosion, so that at points thinning of the vessel wall may give rise to aneurysmal bulging or possibly a true saccular aneurysm. An equally characteristic alteration observed is cellular infiltration about the mouths of the branches of the arch, with, it may be, a distinct narrowing of the innominate or left carotid or more or less occlusion of the coronaries. In the earlier stages the vessel is perhaps but little dilated or deformed, so that the aortic shadow in the roentgenogram may display no alteration in form. It will be obvious that until there is some dilatation or alteration of curve, or at least some abnormal pulsation of the vessel, Roentgen diagnosis is not available. In consequence of this fact, the *x*-ray cannot be relied upon for the detection of aortic syphilis in the early stage. By way of illustration of this fact, we may consider briefly the case of W. B., a colored waiter, twenty-one years of age. This man complains of a persistent aching pain in the left shoulder of about two months' duration. It does not vary much in severity, although he states that sustained activity increases it somewhat, and may develop a dry paroxysmal cough and at times palpitation. Another suggestive symptom is recurring substernal soreness. His general health has, in the main, been satisfactory, and he has continued his occupation with no greater penalty than some aggravation of his symptoms on exertion. He acknowledges syphilitic infection two years ago. Upon examination, the interesting fact develops that firm pressure over the manu-

brium sterni causes a deep-seated aching soreness which persists for some time after pressure has been withdrawn. His heart is normal in size, but on listening to the heart sounds we find along the left border of the sternum a faint diastolic whiff. The blood-pressure is systolic 155, diastolic 85, pulse-pressure 70. The blood Wassermann test is positive. This man's symptoms and physical findings leave us in no doubt that he is developing aortic disease. The blood-pressure picture, diastolic murmur, the peculiar subjective phenomena, and positive Wassermann establish that beyond reasonable question. The *x*-ray plate (Fig. 219)

Fig. 219.

which I show here fails, however, to reveal anything of significance. The heart is normal in size and shape, and there is no change either in width or outline of the aortic shadow. There is not the slightest reason in such a case why we should admit that the negative *x*-ray evidence detracts from the value of our clinical conclusions. The man's syphilis is comparatively recent, about two years, and changes in his aorta have not yet advanced to the point of producing either stretching or bulging. I may add, by way of support to the diagnosis of aortic syphilis, that active antisyphilitic treatment has gradually improved his subjective discomforts,

although, of course, the physical findings remain the same. In this case we are dealing with aortic syphilis in its earliest clinical stage. It is comparatively rare that we have the opportunity of so clearly appreciating this form of syphilis as is offered us by this example. Aortic syphilis ordinarily has a long latency, during which the symptoms, if any, are so obscure or so trifling as to seldom arrest the attention. This has given rise to the belief that syphilitic aortitis is a late development in syphilis, but I am inclined to think that this is more apparent than true, due partly to the symptomatic latency of the infection and partly to our

Fig. 220.

lack of thoroughness in examination and carelessness in the interpretation of slight symptoms. The vast majority of cases coming under clinical recognition are in mature syphilitics, the average duration of the syphilis being probably fifteen to twenty years before the development of severe mechanical defects, such as aneurysm, aortic regurgitation, or angina pectoris. From all that we know of the life history of sclerotic processes it needs no argument to convince one that slow destructive processes must have been at work for a long period to produce the profound disturbances which bring the majority of these cases under clinical

observation. Yet it is not always the slow process that ordinary clinical experience would indicate. Occasionally a case will be observed where the progression of events has been rapid. Longcope reports an instance where rupture of the aorta occurred three months after the primary lesion, and Brooks records instances of rapid development within a few months after infection. I show here in this connection a roentgenogram taken eighteen hours before death (Fig. 220). This shows a greatly enlarged heart, increased in both long and broad diameters; the aortic shadow is increased in breadth and elevated, reaching as high as the sternoclavicular angle, and the lungs are suffused with a dense hypostasis. The patient who furnished this illustration was a colored porter aged twenty-five; he had a luetic infection five years before death and, like many colored syphilitics, he received no systematic treatment. He remained in, what appeared to him, satisfactory health until about ten days before coming to the hospital, when, one evening on his way home from work, he was overtaken by severe precordial pain and intense dyspnea. Although these symptoms abated somewhat in severity, he was unable to lie down with comfort, coughed much, and the slightest exertion caused distress. Upon his admission to the hospital he was found to have aortic insufficiency, relative mitral regurgitation, and pulmonary hypostasis. The heart was enormously enlarged, the blood Wassermann positive. He died one week after entrance; no autopsy was obtainable. This case furnishes us an illustrative instance of how rapid the progression of aortic disease may be. The determining factor of how soon aortic change may come to light in syphilis is not the duration of the syphilis, but the activity of the process in the aorta.

We have no easily recognizable clinical criterion that we can bring to bear for the recognition of aortic change. It is a curious and important clinical observation that the aorta may be greatly degenerated, although the peripheral arteries apparently remain normal. The tones at the base of the heart yield us, perhaps, some information of value, and yet not every direct aortic murmur in a syphilitic, nor, on the other hand, every reverberant second aortic tone, point indubitably to syphilitic disease. It is possible for the

mature syphilitic to have enough senile change of simple sclerotic character in his aorta and aortic valve to give rise to these manifestations. As the matter stands at present the *x*-ray constitutes the best source of information that we can bring to bear in the identification of these cases.

We shall not be in a position to intelligently employ the *x*-ray in estimating the amount of damage done to the aorta unless we are already familiar with the appearance of the adult aortic shadow in health and in the more common non-syphilitic diseases; in other words, we must have a standard for comparison. For example, some dilatation of the aorta is one of the most common findings in roentgenography of the heart. It is practically always present in high blood-pressure states, in nephritis, and arteriosclerosis. It often exists, on the other hand, as the only characteristic of the aortic shadow in syphilitic aortitis. Interpretation in such cases rests upon serologic findings, the clinical history, etc. No arbitrary interpretation of alteration in outline is, of course, justified. It is only when all facts are assembled that definite conclusions should be drawn. The dilatations of the aorta resulting from syphilis may assume a variety of forms depending upon the extent and severity of the inflammatory process; thus, when the infection is localized at some particular point, a focal bulging may develop, whereas if it is widely diffused and not very active, a general dilatation of the vessels is likely to follow. Sometimes the dilatation is irregular, giving the impression of two or more fusiform aneurysms. Again, it may result in a single typical fusiform aneurysm, while in still other instances sharply focal lesions lead to the formation of one or more saccular aneurysms.

Let us consider for a moment the normal aortic shadow in the roentgenogram (Fig. 221). It will be seen that it lies in its first portion behind the sternum and does not project beyond the right auricular curve. At the arch where it curves backward and to the left there appears a more or less well-rounded knob to the left of the sternum well above and distinct from the cardiac shadow. This so-called "aortic knob" may well merit special attention, since it is one of the striking anatomic peculi-

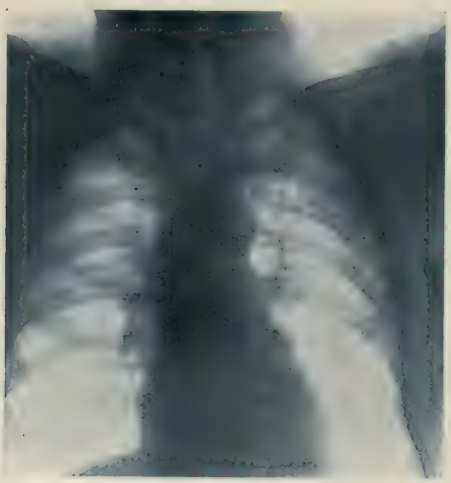


Fig. 221.

arities of this area, and its alteration in form possesses some value in diagnosis. This knob is not equally well defined and prominent in all normal aortæ. It may be so prominent a feature as to be mistaken for an aneurysm (Fig. 222), whereas in the asthenic pear-shaped or "dropped" type of heart it may hardly show at all (Fig. 223). It varies in prominence according to age, being less well defined in early life than in adults. In the aged and senile sclerotic the shadow is apt to be pretty sharply outlined, its edge intensified by sclerous thickening and lime deposit (Fig. 224). It is less apt to be a prominent feature in adult females than in males of corresponding age. It may not be necessary to emphasize the fact that a certain amount of varia-

Fig 222.

Fig. 223.

Fig. 224.

tion from the normal is common in health. That is true of all features of cardiac roentgenograms. It can hardly be said that there is a fixed type of normal heart; the heart fits the body.

In one healthy individual it may be a short, rather wide heart, with a relatively broad aortic shadow, and in the next healthy individual of equal age, who has a longer chest and a lower vascular tone, the roentgenogram may show a heart of long type with a narrow aorta.

In aortitis the *x*-ray reveals two kinds of change, namely, alteration in density of shadow and change in contour. In early aortitis the pathologic process is almost invariably localized to the first portion of the aorta near the aortic valve. As

Fig. 225.

the vessel at this stage is but slightly thickened, there may be merely a doubtful dilatation of the first part of the arch, with exaggerated pulsation at that point. In such cases the heart is rarely enlarged; with the progression of the aortitis the artery becomes more and more dilated, and as a result the aortic shadow as it ascends from the heart is widened, so that it projects beyond the outline of the curved right auricle (Fig. 225). In most instances the shadow is regular, but it may display slight bulging or protusion. Should dilatation extend to the transverse arch, the knob may lose its well-defined curve, becoming flattened and

broadened. These, in outline, are the anatomic features of the simple type of syphilitic aortitis. Aneurysms should publish their presence by alterations of curve that immediately arrest attention. It hardly requires emphasis at this day that the *x*-ray furnishes the only reliable means which we possess of detecting small aneurysms. While in the earlier stages of aortitis Roentgen evidence consists merely of increased curvatures, dilatation, and abnormal pulsation without notable increase in the size of the heart, we find sooner or later as time goes on more or less characteristic change in the size and shape of that organ. In the later

Fig. 226.

stages of aortitis the heart constitutes one of the most characteristic features of the roentgenogram. An increase in size develops gradually whether aortic insufficiency is present or not. This increase effects to a much greater degree the long diameter than the broad diameter of the heart, the heart assuming a position more nearly horizontal than normal, producing a boot-shaped shadow. This type of heart shadow is very similar to that seen in high blood-pressure states. The marked pulsation of the left ventricle seen on the screen in hypertensive states is less emphasized in aortitis. This type of heart has been termed the aortic heart (aortic configuration, Fig. 226) in contradistinction to the

broad or bag-shaped heart of mitral disease (mitral configuration). The spread of the disease to the aortic valve with the production of aortic insufficiency greatly augments the heart shadow, and its horizontal configuration is correspondingly magnified. In advanced cases relative mitral insufficiency is superadded, with the effect of producing an enormously bulky shadow, the true cor bovinum. Good examples of this, the cardiac end-product of aortitis, are the two plates that I show you (Figs. 227, 228). One of these (Fig. 227) represents the heart of a man who was put to

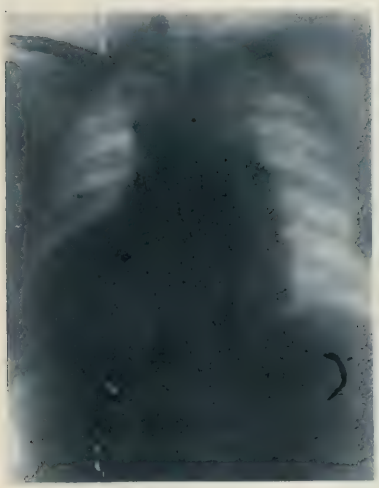


Fig. 227.

Fig. 228.

bed in the hospital eighteen months ago with a badly ruptured compensation. He was markedly edematous and had much pulmonary hypostasis and the cardiac signs of insufficiency the result of syphilis of fifteen years' standing. I refer to his case because this man is still living and during the past winter has been employed as a Pullman car conductor. I must say that it is rare to see a patient who has advanced to the point of cardiac decompensation with aortic insufficiency, reduced to so extreme a state as was this man during the summer of 1916, live so long a time and regain his activities. Ordinarily, developments of this

character warrant the most serious prognosis, for it is well known that aortic insufficiency of syphilitic origin does very badly, the prognosis being vastly graver than in non-specific types of aortic disease, probably because the lesion is progressive and the myocardium ordinarily placed at disadvantage because of coronary involvement. While we are mentioning coronary involvement in syphilis, it is interesting to refer to a patient recently under observation, a plate of whose heart I now throw on the screen (Fig. 229). This man, fifty-four years of age, contracted syphilis twenty-five years ago. Being a man of means and intelligence,

Fig. 229.

he secured what was considered at the time adequate treatment, and was assured at the end of three years that he was cured. A few months before I saw him he developed pain in the precordium following exertion. At first recurring at considerable intervals, these attacks grew in frequency until it was impossible for him to carry on his affairs because any exertion beyond the simplest character brought on severe pain. The pain was accompanied by a sense of iron-like constriction across the chest, severe dyspnea, and a sense of suffocation. These symptoms yielded promptly to nitrites and rest. Upon examination of his heart

it was found to be enlarged, his blood-pressure elevated, and he had an aortic direct murmur. The Wassermann was positive. The interesting feature of this man's case is that after six weeks spent in the hospital with intensively administered antisyphilitic therapy comprising, among other measures, 2½ grams of salvarsan in small doses at three-day intervals, his heart pang entirely disappeared, and for two months he has had no attack, although during this period he has made a long railroad journey and has indulged in moderate activities. The syphilitic origin of angina pectoris is, of course, familiar. That so marked benefit may accrue from antisyphilitic therapy in this condition opens an encouraging prospect for many of these poor sufferers.

That so marked an improvement secured in the case cited was not coincidence or accidental happening would appear from my experience in other cases, notably in the case of an old syphilitic who at the age of sixty-five developed angina pectoris so badly that he was completely invalided, so slight an exertion as turning in bed without the assistance of the nurse being sufficient to precipitate an attack. Despite the discouragements offered by so extreme a development, an attempt at specific relief was made by administering ½ decigram of neosalvarsan intravenously every third day. After the third dose slight improvement was observed, and the treatment was continued with gradual increase in dosage. A dose of 3 decigrams was finally reached, with so good effect that his attacks declined in frequency and abated in intensity, so that he was able to be out of bed and about his apartment and lived in fair comfort for a number of months before he died. If due care is exercised in carrying out antisyphilitic therapy in angina pectoris, it seems to me that it should always be attempted. I need not insist that the first dose should be very small and subsequent injections regulated by the reaction following that preceding.

The vast majority of cases that come under clinical recognition for syphilitic aortitis have passed through the latent stage and developed symptoms referable to the circulation. The methods of physical examination in these cases will usually reveal some alteration of the heart or change in the circulatory

rhythm or blood-pressure, but it may not be apparent that syphilis is the underlying cause until the point is inquired into or the blood examined for the Wassermann. Even should the Wassermann test prove positive or the man confess syphilis, the conclusion is not at once obvious that his circulatory disturbance is of syphilitic type, since there is no exemption among syphilitics from blood-pressure and myocardial defects resulting from causes quite other than syphilis. The shape of the heart and especially of the aorta as revealed by the *x*-ray may convert the probability of the case being syphilitic almost into a certainty, should it prove typical.

The next case that I have to show you may serve to illustrate how a case of this kind may work out. This man is forty years of age and his chief complaint is uncomfortable heart action. He has much belching and is greatly troubled by irregularity of the heart, especially at night. His general condition is characterized by a lassitude and lack of endurance, which is very different from his former habit. He confesses to syphilitic infection occurring eleven years ago, for which he took treatment covering a period of two years. He has had several Wassermanns made on the blood, all of which have been reported negative. Physical examination reveals an enlarged heart, and with the stethoscope can be heard a rough short systolic murmur in the aortic area. There is a premature contraction arhythmia and his blood-pressure is systolic 210, diastolic 150. Signs of an early tabes exist, the pupils are very sluggish to light, the ankle-jerks are absent, and he has a slight Romberg. The urine contains albumin and casts, the renal function with the phthalein test being 60 per cent. The clinical diagnosis in this man's case was syphilitic myocarditis, nephritis, and tabes. The roentgenogram (Fig. 230) shows a typical aortic type of heart with a diffuse dilatation of the aorta. I am sorry we have not the spinal fluid findings in this case. It is not improbable that we would find the Wassermann positive in the spinal fluid. I have no doubt in my mind that the organic conditions here are all of syphilitic origin, and I am particularly glad to show you this case because it represents a not infrequent experience of encountering late syphilitic develop-

ments, such as tabes, aortitis, and myocardial disturbance, in an individual who has a negative blood Wassermann. We are not to pin our faith too absolutely to the findings of the Wassermann reaction; there is a margin of error quite wide enough (40 per cent.) to lead us astray if we dismiss the idea of syphilis on a negative laboratory report. Experienced clinicians will not make this mistake, and we should all be a little more tenacious than we are in upholding our clinical diagnosis when we find it opposed by the laboratory reports. After all is said and done, there is no

Fig. 230.

criterion in medicine more reliable for diagnosis than the information secured by careful clinical history and painstaking physical examination. One or two points in this case may delay us profitably. The peculiar lassitude and depression which constitutes the chief complaint of this patient is a symptom occasionally noted in aortitis, and is interpreted by Albutt as significant of coronary involvement. Another point of interest to be noted is the association of aortic disease with signs of developing tabes. This is an association not infrequently noted in literature. In manifest tabes Stadler found aortic disease in almost all cases.

He regarded so-called cardiac crises as being, in reality, angina pectoris due to coronary stenosis. In this connection I show you the aorta of a patient who recently was in one of our wards (Fig. 231). He was picked up by the police ambulance and brought to the hospital. He had been seized while on the street with a severe pain in his chest and had fallen to the pavement. When he was admitted he was manifestly in severe pain, was extremely pale, and distressed in appearance. The pain was referred to the chest, was described as an iron-like constriction, and he breathed

Fig. 231.

with difficulty. Nitrites failed to give him relief and morphin was administered, but it was not until after twelve hours had elapsed that he was again comfortable. This was not the first attack of that character that the patient had had, but was the most severe; it usually lasted several hours, was not induced by exertion, and was not accompanied by vomiting. Upon examination, he was found to have an enlarged heart, a practically normal blood-pressure, a wide aorta, and the characteristic signs and spinal fluid of tabes dorsalis. We experienced some difficulty in deciding whether the attacks of pain were genuine angina

pectoris or cardiac crisis of tabes, but decided in favor of the latter after having kept him in the hospital for a number of weeks without any recurrence of pain, although he was permitted to indulge in very considerable activities. I need not emphasize the difficulty that must necessarily surround the decision, especially between attacks, of this point. History of the case and the stage to which the tabes has developed will prove important factors in the proper evaluation of the cardiac pain. In general, with well-advanced tabes, anginoid symptoms are more apt to be

Fig. 232.

cardiac crises. With tabes latent and the aortic disease well developed anginal seizures will more probably prove of true cardiac nature. In general, the symptoms of aortic disease appear later than tabetic manifestations. This is, perhaps, not because aortitis is a later development, but only that it has a longer latency than tabes.

I cannot refrain from citing a case recently observed in private practice, especially as I have Roentgen plates for your inspection. The patient was a white man, aged thirty-two, married, with two children, one of them living and healthy. He de-

nied ever having had a syphilitic infection and had always enjoyed the best of health. He had been active and robust until three months before he came under my observation, when, following exertion, he developed dyspnea, cough, and palpitation. Seeking professional advice, he was told that he had a heart disease, although its nature was not suspected. Upon examination, his heart was found very much enlarged, there was present the diastolic murmur of aortic insufficiency, his blood-pressure being 200 systolic and diastolic 80; the blood Wassermann typically positive. The roentgenogram, as you will see (Fig. 232), shows a heart shadow increased in both length and breadth; the shadow of the aorta is much widened and rises high in the chest. The second plate, taken in the anterior semilateral position, shows beautifully this great thickening of the heart and increased aortic width. I refer to this case not because it is an essentially rare one, but because it represents an observation we may any of us encounter in clinical work at any time. Except in the item of the man's ignorance of his lues it differs in no way from any individual who develops aortic insufficiency in adult life without antecedent endocarditis. Experienced clinicians know very well the nature of these cases of aortic insufficiency developing in the adult, but to many it will require emphasis. Every individual displaying aortic lesions who does not give a clear history of rheumatic endocarditis should be at once suspected, whether he avows it or not, of having syphilis, and a Wassermann should forthwith be made.

I shall conclude this series by presenting to you the case of R. W. to illustrate the difficulties sometimes encountered in the diagnosis of aneurysm resulting from syphilitic aortic involvement. This patient, thirty-four years of age, entered the hospital for relief from a severe paroxysmal cough. The cough had a suspicious strident, unproductive character, was worse at night, interfering with sleep, and there was a good deal of hoarseness. The cough was little influenced by exertion, but decidedly aggravated by the recumbent position. His general health was excellent. He confessed to having a syphilitic infection ten years ago. Aneurysm of the aorta was suspected; indeed, it was the "exam-

ining-room diagnosis" based upon the character of the cough, but not supported by any convincing physical signs. All that physical examination revealed was an obscure systolic murmur at the inner edge of the left scapula just above the inferior angle. The heart and chest were otherwise negative; no physical signs of aneurysm could be detected except that the laryngoscopic examination showed left vocal chord paresis. The blood Wassermann was strongly positive. When we came to examine this man's chest with the *x*-ray we were greatly disappointed not to find anything to support our diagnosis. A number of plates showed

Fig. 233.

absolutely nothing; the heart was normal in size and contour. Finally, upon subsequent examination, we got a good plate of the aorta in the semilateral position (Fig. 233) which decided the matter beyond question. You will see by this plate that there exists a well-marked aneurysmal dilatation of the posterior aspect of the transverse portion of the aortic arch. Its position furnishes the key to the pressure cough which plagues this patient and renders easy of understanding why recumbency so greatly aggravates his discomfort. An aneurysmal bulging of this size might exist almost anywhere else without causing any symptoms,

indeed, we know that not only small bulgings but saccular aneurysms of large size may develop without the patient having any symptoms whatsoever, constituting the so-called "aneurysm without symptoms." An aneurysm placed as this one unfortunately is need not be of large size to produce the most disturbing symptoms, somewhat in the same manner as a small retrosternal goiter pressing upon the trachea may make life miserable, whereas a large mediastinal growth exerting lateral pressure may hardly publish its existence.

Fig. 234.

If you will for a moment inspect the last of this series of plates (Fig. 234) you will see a large aneurysm of the transverse portion of the arch extending, as such bulgings usually do, to the left, so that the aneurysm in this case fills a considerable portion of the dome of the chest. The patient who has this aneurysm entered the wards for diagnosis. Being an intelligent man, he had become skeptical of the existence of a chronic tuberculosis which had been diagnosed in his case, and for which he had been treated for six months in a tuberculosis sanitarium. For almost a year he has had a cough, with a moderately copious catarrhal expectoration.

Beyond this single symptom there had been no complaint except to note a gradual loss of flesh. An aneurysm apparently had not been suspected. An *x*-ray had never been made of the chest. Physical examination revealed a dull area corresponding to the shadow shown on the plate, with many moist râles throughout the left chest. The mass when observed on the screen was seen to pulsate with a distinct expansile pulsation. Quite recently, through the courtesy of a friend of mine, I saw the chest plate of a patient who had an enormous aneurysm of the first part of the arch which filled entirely the area ordinarily occupied by the upper lobe of the right lung, causing its complete collapse. I was assured that this state of affairs had given rise to no symptoms whatsoever referable to the chest, and had been discovered quite accidentally while screening the patient during the course of a routine gastro-intestinal fluoroscopy. Direction in which pressure is exerted by the aneurysm and the rapidity with which the dilatation occurs and grows are undoubtedly determining factors in the production or absence of symptoms.

In our discussion this morning we have reviewed in a somewhat desultory way certain of the important considerations in connection with syphilis of the aorta. Many points of necessity have not been touched upon. I have sought rather to bring out the leading clinical features. My desire is to particularly impress upon you the importance of the aortic manifestations in chronic syphilis. The character of the material one handles undoubtedly plays a considerable part in cultivating interest in this feature of syphilis. In large urban centers with a considerable proportion of negroes in the population aortic syphilis will have a much greater incidence and come more frequently under observation than in less congested areas with a population of less mixed type. The colored race, perhaps because of some undue susceptibility of vascular tissue and probably also to some extent because of carelessness in their attitude toward treatment, when they acquire syphilis, which they do as is well known very frequently, furnishes us a larger proportion of syphilitic aortic degenerations than any other class. Lenz makes the statement that in large cities 25 per cent. of all syphilitics die from aortitis and its conse-

quences, as against 3 to 4 per cent. from paresis, 1 to 2 per cent. from tabes, and 10 per cent. from all other forms of internal syphilis, as of the brain, liver, stomach, lungs, etc. Living in Hamburg, where there is a large sea-going working population, a class proverbially exposed to conditions favoring aortic disease —*i. e.*, syphilis, hardship, hard work—Lenz's statistics may perhaps not serve as a fair criterion for other communities. But, after discount, his statement will serve to emphasize its importance in any industrial center.

Aortic syphilis presents us with a double problem in treatment. Every case that has advanced to the stage of clinical manifestation is a cardiopath, and requires to be safeguarded according to the well-known rules which constitute the hygiene of that class. The special feature of its therapy which interests us today is the treatment of the specific underlying factor. Aortitis is due to localization in the aortic tunics by the spirochete of syphilis, and its progression, with the subsequent developments which mark its course, are the results of the activity of that organism. If we accept this very obvious conclusion, the equally obvious deduction is apparent that we must treat syphilis in the aorta as we would syphilis in the skin or in the nervous system by direct attack with intensive antisyphilitic therapy. If we hope for cure by this method, disappointment invariably awaits us, for the simple reason that aortitis advanced to clinical recognition has wrought serious damage to the parts involved. Aneurysms, scars, dilatations, deformities cannot be cured, but a carefully planned campaign against the spirochete may suffice to control the future progression of the disease and protect the tissues from further damage. As I have indicated by several citations, antisyphilitic treatment is capable of greatly improving the symptomatic comfort of these patients, and even were this all of which it were capable, its guarded yet vigorous employment would be justified.

CLINIC OF DR. JOSEPH C. FRIEDMAN

MICHAEL REESE HOSPITAL

REFLEX GASTRIC DISTURBANCE AND EPIGASTRIC PAIN

Pylorospasm: Meaning of Tenderness in Epigastrium. Origin of Pain in Some Cases of Angina Pectoris.

THE patient whom I wish to demonstrate is forty-one years of age, single, a drug clerk by occupation, and complains of pain in the epigastrium and left side of the abdomen, extending around to the back. It is a burning pain, rather sharp in character, and comes on two to three hours after eating. It is worse just before meals. He has complained of this about ten years rather constantly. He first noticed constipation; then some distress after meals, and more recently the burning sensation above mentioned. He has never had any night pains. All his symptoms have been somewhat exaggerated in the last two weeks, during which time he has lost 5 pounds. The patient's previous history is unimportant except for an appendectomy thirteen years ago.

On examination we see a rather poorly built man in a fair state of nutrition, with a marked kyphoscoliosis of the dorsal region and an equally marked, evidently compensatory, lordosis in the lumbar region. This deformity has been present since childhood and has never given him any trouble. It is evidently due to some general disturbance in this patient, such as rickets, rather than to a spondylitis. The lungs and heart are normal and the abdomen somewhat protuberant. The abdominal walls are rather thin and musculature slightly developed. The spleen and liver are not palpable. There is no abnormal tenderness anywhere in the abdomen. Reflexes are normal. Blood, urine, and temperature are normal. Rectal examination shows a small amount of fecal matter in the ampulla.

As a result, then, of our examination we can only say that our patient has a rectal constipation or a so-called dyschezia. Is this sufficient explanation for the pain? A pain of this sort, coming on more than one hour after eating and being relieved by the next meal, is, as I have frequently pointed out to you, a type of late pain, and, in my experience, indicates just one thing, namely, pylorospasm. The method by which pylorospasm produces pain is known to you. We believe, in short, that the sensory nerves of the gastro-intestinal tract do not respond to the same kind of painful stimuli as the sensory nerves of the skin. The specific pain stimulus of the afferent nerves of the stomach and intestines is an abnormal increase in intragastric or intra-intestinal pressure. Such an increase would be brought about by a contraction of one section of a viscus without the normal relaxation of the segment distal to it. For instance, contraction of the antrum of the stomach without relaxation of the pylorus would cause an increase in pressure in the intervening segment. This increase in pressure is felt as a pain. Such a condition is more apt to arise toward the end of digestion when the pylorus normally tends to close, or when the stomach is entirely empty, and hence the pains of pylorospasm are more apt to occur at this rather than at the beginning of a meal, when the pylorus tends to relax.

The most frequent cause of such late pains is, by all odds, an ulcer situated at or near the pylorus, but it would certainly be an exaggeration to state that this is the only cause, for it is most reasonable to believe that any condition which stimulates the vagus may give rise to pylorospasm, hence, to typical late pain. Such are simple hyperacidity or hypersecretion, adhesions between the gall-bladder and the pylorus, or overirritability of the vagus due to hyperesthesia of the central nervous system, and in some cases a late pain is connected in some way with constipation, probably both being due to an abnormally irritable central nervous system.

With this explanation of visceral pain in mind, let us return to the laboratory examination and our *x*-ray findings. A test-meal was given and withdrawn in portions at intervals of one-

half hour for three hours, showing a maximum free acidity of 20 and a maximum total acidity of 36, with some slight impairment of motility. There was no blood in either the stomach contents or stool. Further examination of the stools showed no increase in mucus, starch, fat, or meat fibers.

The *x*-ray report is as follows: The stomach is hypotonic, the greater curvature coming down to within four fingerbreadths

Fig. 235.—Arrow indicates bulging on greater curvature. Taken forty minutes after ingestion of barium.

of the symphysis. Peristalsis is normal, the waves starting high up on both curvatures. The antrum cuts off well; there are no gastric defects. The bulbus duodeni fills readily, is regular in outline, and freely movable. At one point on the greater curvature in the cardiac portion of the stomach about one-third of the distance between the lowest point and the cardiac orifice is a bulging which changes with the respiratory rhythm, being

most marked during the expiratory phase and disappearing during inspiration. It is quite independent of the peristaltic waves, and gives the impression that this point is being held down when the stomach rises during expiration, the pull being relaxed during inspiration (Fig. 235). In six hours the stomach was empty. The barium column has reached the terminal ileum

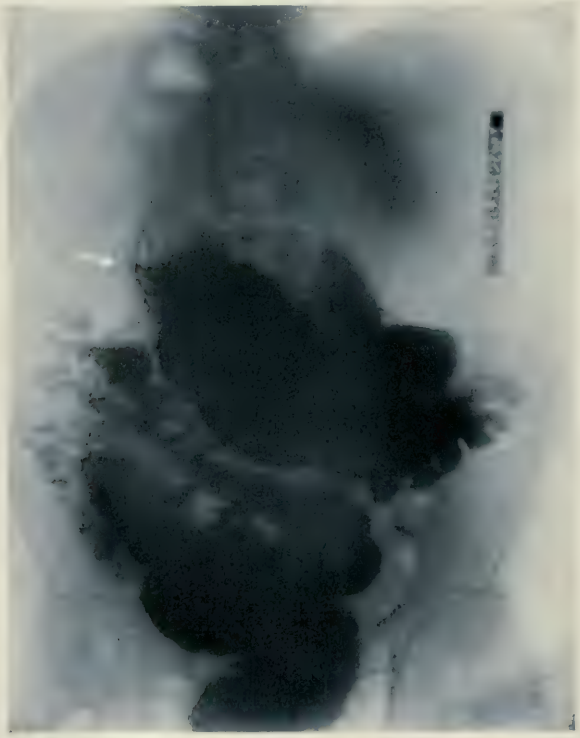


Fig. 236.—Barium per rectum and by mouth, showing relation of bulging on stomach wall to colon.

and is collected in the pelvic ileum. In twenty-four hours it has reached the rectum. The colon appears movable throughout, but the cecum is not well filled at this time. The descending and sigmoid colon show now only as a narrow ribbon. The splenic flexure is low as well as the hepatic flexure; the former when the patient is upright being below the crest of the ilium.

A barium enema was given, the patient was again given barium by mouth, and it was then seen that the prominence on the greater curvature was due to a pull on the stomach by the splenic flexure, the latter being, as stated above, abnormally low in the abdomen, but not abnormally fixed (Fig. 236).

The result of the *x*-ray examination, then, is a very marked visceroptosis, with a marked dropping of the splenic flexure as well as the hepatic. The latter condition, namely, the dropping of the hepatic, being quite frequent; the former, namely, the low position of the splenic, being somewhat unusual, due, of course, to a relaxation of the phrenicocolic ligament, with no corresponding relaxation at the left gastrocolic omentum, resulting, at each respiratory phase, in a pull on the greater curvature of the stomach, and hence causing the prominence above mentioned. Can this cause a gastric disturbance? I would not have placed much stress on the possibility had I not, a few months before, seen an exactly similar occurrence with similar symptoms, and this case I wish to report to you somewhat in detail.

The patient is a young married woman who has been complaining for five years of considerable abdominal distress. This consists of a feeling of fulness in the abdomen, relieved by soda, and also relieved by passing flatus. She has no real pain, but sometimes has a heart-burn one to two hours after eating. She has no night pains, and during this same period of time has had a constipation gradually increasing in intensity. Seven years before she had had a left nephrectomy for pyelitis. On looking up the operation, it was found that the left kidney was adherent to the colon, and that during the operation the colon had to be peeled off from the kidney for a considerable distance. Her appetite is good, she has lost no weight, and except when she has the abdominal distress feels perfectly well. The physical examination is negative. The stools reveal nothing abnormal. The stomach contents show a maximum total acidity of 72, maximum free of 42, with good motility. The *x*-ray report is as follows:

The stomach is hypotonic, the greater curvature being three fingerbreadths below the crest of the ilium. Peristalsis normal, antrum cuts off well, bulbus duodeni fills well, is sharp and clear

in outline and movable. On the greater curvature, at a point about two fingerbreadths below the indentation of the left costal arch, is a bulb or pouch which is quite independent of the peristaltic waves and which increases on expiration as the diaphragm rises, and decreases during inspiration with the descent of the diaphragm (Fig. 237). This pouch suggests adhesions of the

Fig. 237.—Mrs. S. Arrow points to bulging on greater curvature. Fluoroscopically it was more marked than this plate indicates.

stomach at this point, pulling the stomach out, rather than a filling defect. In six hours the stomach was empty. The barium had reached the ascending colon. In twenty-four hours the barium had reached the rectum, the ampulla containing a very large amount. The hepatic flexure is low; the splenic flexure is in the normal position. In the ascending loop of the splenic flexure is an area of constriction due either to spasm or to ad-

hesions connecting with the pouch on the greater curvature of the stomach. The cecum is somewhat immobile. In forty-eight hours the colon presents the same picture at this time as at twenty-four hours, with the exception that there is less barium present. An opaque enema was given two days later after the bowels had been emptied from the barium meal. The colon then

Fig. 238.—Barium enema with barium in stomach, showing adhesions between the two.

filled readily throughout, revealing no defect. Some barium was given by mouth at this time, and it was then apparent that the ascending loop of the splenic flexure is in close relation to the stomach, especially at the point of defect which presents itself on the greater curvature as in the first examination. It is impossible to separate the stomach and colon at this point, as they are apparently firmly united (Fig. 238).

To sum up our findings then: We have a patient who, a few months following a nephrectomy, seems to have abdominal distress and an increasing constipation, with a late pain or, rather, a heart-burn. Our clinical findings are hyperacidity. Our radiographic findings are adhesions between the splenic flexure and the greater curvature of the stomach, with some spastic condition of the former and an intermittent pull on the latter. My explanation of the constipation would be that it is of a spastic type resulting from some stimulation of her colon and causing a collection of gas at the point of spasm, also interfering intermittently with the onward movement of the fecal column. The adhesion to the stomach results in an irritation of the vagus and a consequent hyperacidity, and also in the pylorospasm, and I believe that exactly the same interpretation can be given to the findings of the patient I am presenting to you, the difference being that the abnormal pull is due to a descent of the splenic flexure instead of being the result of an old inflammatory process.

There are, however, several points in the history which need further discussion. The first is the meaning of abdominal and, in particular, of gastric distress. Our interpretation here depends on the time at which the distress appears. It is, as you know, a most frequent complaint in visceroptosis, and characterized here for the most part by its occurrence immediately on taking food. Here, as usual, the abnormal sensation must be interpreted in terms of abnormal intragastric or intra-intestinal pressure. The most reasonable theory is that in the normal individual as food enters the stomach the muscle-fibers relax in order to accommodate the increase in contents. In the lower animals we know that this relaxation may amount to three times their tonic length. In a visceroptotic and atonic stomach this relaxation, however, is constantly present; therefore, when food is introduced, no further relaxation can occur. Consequently, the individual gets the sensation of an already filled stomach, that is, a sensation of fulness, and the desire for further food is lost. If the feeling of fulness occurs one or more hours after eating, it has exactly the same meaning as a pain in the epigastrium or as heart-

burn; that is, it is due to a rise in pressure, generally in the antrum, and, as stated above, is caused by abnormal closure or absence of relaxation of the pylorus; in other words, a pylorospasm.

Pylorospasm, then, may result in all grades of discomfort, from a slight feeling of fulness to a heart-burn, or to an intense pain, the degree of discomfort evidently depending on the varying increase of intragastric pressure. It must be remembered, however, that in the three to six hours following a meal the food is passing through the small intestine, and a spasm resulting in a local increase in pressure may arise consequently in any part of the small intestine during this time, and hence we may get a typical late pain through the spasm if there is a lesion in any part of the small intestine, so that all late pains are not necessarily due to lesions in the stomach, but may just as well be due to lesions in other parts of the intestinal tract at the time of their greatest activity. For instance, I remember one patient who had an intense pain in the pelvis one hour after eating, and at operation a massive adhesion between the omentum and the pelvic ileum was found as the result of an old pelvic peritonitis. Here, evidently, the peristalsis of the stomach exerted a pull on the ileum through the omentum, causing irregular contractions and, consequently, quite severe pain. The patient was and is still relieved by the operation.

Intestinal distention, then, may result in all grades of discomfort, from a slight distention to the most severe colic. What is it that determines the degree in any given individual? Unquestionably the most extreme grade of increased pressure or spasms will be interpreted as pain by all individuals, but in the milder grades unquestionably a great deal depends on the sensitiveness of the nervous system of the patient, and what is a simple distress in a phlegmatic individual will be interpreted as a severe pain in a hyperesthetic or so-called neurasthenic individual, that is, one with an unstable sympathetic system. A good example of this is the condition so often seen in the involution psychoses. A common complaint here is of a pain or discomfort which feels as though it were traveling around from one part of the abdomen to the other. In such an individual whom I re-

cently fluoroscoped the cause of the discomfort was evident. There was very marked hyperperistalsis of the stomach and the whole of the small and large intestine, so that within thirty minutes the whole of the small intestine and the large intestine to the hepatic flexure were filled with the barium meal. It was this unusual distention which caused the patient discomfort.

Such a condition is not unusual after gastro-enterostomy, but whereas in those conditions the patient complains simply of a feeling of fulness after eating, in the psychasthenic individual the feeling of fulness was interpreted as unbearable distress. We must, then, in interpreting the severity of this condition always consider the nervous reaction of the individual.

Another point in the history of our patient is the increasing constipation. You will remember that the *x*-ray report tells us that the barium was in the rectum in twenty-four hours after ingestion; that at that time the descending colon and sigmoid were spastic in their turn, showing only as a narrow ribbon. The perfectly normal onward movement of the barium column is the usual finding in a patient of this type. As you know, the average time for the barium to reach the cecum is four and a half hours; the hepatic flexure, six and a half hours; splenic flexure, nine hours; the pelvic colon, eighteen hours, and the rectum, of course, within twenty-four hours. The delay, then, must be in the final act of defecation, and this, as I said above, is the rule in visceroptotic individuals. Constipation in such individuals is not due to kinks and twists at the flexures, as Lane and so many others believe, but is simply due to an inability of the abdominal muscles to play their part in the final act. It is, then, not a colon constipation, but a rectal constipation or so-called dyschezia. The futility, then, of attempting to overcome the result of this type of sluggishness by excluding the colon is obvious. Other means must be used. The ribbon-like sigmoid is a frequent complement of this condition. Unquestionably, it is generally due to a reflexly irritated bowel either from the constant presence of stool in the ampulla or from an overirritable central nervous system. I think in the present case it is fair to believe that some of the spasticity at least may be due to the unusual pull from

the stomach, just as we interpreted the gastric spasm as partly due to the unusual pull from the colon.

With these facts in mind the treatment is simple. We shall try to place the colon in a more favorable condition in order to relax the pull of the stomach wall. A properly fitted binder with a pad in the left lower quadrant placed in position while the patient is reclining with hips elevated is the first necessity. The second is a strengthening of the abdominal muscles by appropriate exercises, such as lifting the body from the reclining to the upright position by the trunk muscles alone; lifting the legs from the reclining position to the upright, bending forward and backward, etc., are of very great assistance. Massage is not indicated here, because we already have a spastic colon and manipulation would only increase this condition. The diet should have two considerations: first, the atonic stomach, and second, the spastic colon. The atonic stomach requires us not to overload it at any time. Meals should, therefore, be concentrated and dry, fluids to be taken between meals only. All foods should be very thoroughly cooked and soft. All mechanical irritants, such as cellulose, should be reduced to a minimum. No further attention need be paid to any balance of the different constituents except the instinct or the desires of the individual. It must always be borne in mind that the condition of the central nervous system has an important bearing on the functioning of the gastro-intestinal tract, and these conditions may remain latent until called forth by some unusual mental strain.

For the actual relief of the constipation cathartics are contraindicated. There is only one exception or partial exception, and that is milk of magnesia when the patient has a hyperacidity; then such a mild cathartic which neutralizes the acidity is not contraindicated. Strong ones, by increasing peristalsis, only make matters worse. The best treatment, unquestionably, is the old one of oil enemas of 4 to 6 ounces, to be retained throughout the night; then gradually leaving out two or three nights a week until only an occasional one is necessary.

The patient with the nephrectomy under such treatment has remained well with an occasional relapse since the beginning of

treatment. If necessary, we may give belladonna and bromids for a short time to further diminish spasm. They must, of course, be given to the physiologic limits in order to produce any results.

It is my firm conviction that operative procedure is indicated in adhesions only when the necessity is unusually urgent; continuous vomiting, for instance, or a constipation bordering on obstruction might drive us to such interference, but certainly when we know that the separation of adhesions is likely to be followed in a few months by the formation of still firmer ones, we should exhaust all our other resources before taking refuge in surgery.

CASE NUMBER TWO

The second patient has some points of similarity with the preceding one, as well as some striking differences. He is sixty-nine years old, married, and has been a very active man all his life. He complains of pain in the epigastrium, discomfort in the same situation, belching and loss of weight, the latter amounting to 82 pounds in five years. He has had his pains in the epigastrium for several years. They extend upward under the sternum and backward between the scapulæ. They come on one to two hours after meals, often accompanied by nausea, but never by vomiting. At times he is awakened at night with the pain. Almost always after eating he has a sense of discomfort in the stomach almost immediately, which he describes as a tightness or a sense of constriction. The pains are made worse by walking, but are not particularly relieved by lying down. There is marked relief by belching and by taking some warm fluid. They last from twenty minutes to three hours. His appetite is good, but he is afraid to eat. He has discarded various articles of diet, such as cereals, many other carbohydrates, meat, as he believes that they may be responsible for his pains. As a consequence he has been living on broths and milk and a few soft foods for some time.

Past History.—He had pneumonia twenty-six years ago, typhoid forty-eight years ago. Forty-five years ago he had a severe diarrhea with mucus in the stools lasting for about a month. He has been a heavy smoker, but a very moderate user of alco-

hol. The last four or five years small amounts of sugar have been found in his urine at times. He has coughed, especially in the morning, for many years, and at such times has expectorated freely, but never any blood. Denies all venereal infection.

On examination, we see a well-built, somewhat emaciated man, whose lips are slightly bluish, whose tongue is quite dry and red. His pulse is full (96), regular. Arteries show no marked thickening. Lungs are normal. The heart outlines are normal, sounds are quite weak, no accentuations, no murmurs. Blood-pressure 145 systolic, 65 diastolic. The abdominal skin is very loose, with a lack of subcutaneous fat. No abnormal peristalsis. No tumors. There is some tenderness in the mid-epigastrium and over the xiphoid. There is no rigidity. The tenderness is not a skin hyperesthesia, but obtained only on deep pressure. Some succussion found extending to two fingerbreadths below the umbilicus. Elsewhere no tenderness. Spleen, liver, and kidneys are not palpable. The reflexes are normal and there is no edema in the extremities. Sputum examination: No tubercle bacilli found. Stool somewhat constipated, dark. Benzidin test positive. Guaiac negative for blood. No increase in mucus. There was some increase in starch granules. No test-meal was given because of his weakness. A blood Wassermann was negative. Urine on entrance 1024 specific gravity, a trace of albumin, and an occasional hyaline cast. No sugar. Blood examination normal.

To sum up the history and the findings as thus far given: There is a pain in the epigastrium definitely related to the taking of food, consisting of a distress immediately after eating, and also a severe pain one to two hours after eating, especially after he has exerted himself. Then, sometimes, a pain awakening him at night, relieved by belching or by passing gas. There is marked tenderness in the epigastrium and over the xiphoid, the whole suggestive of some gastric disturbance. This has lasted many years and his appetite has remained good. This is apparently not a very malignant process, possibly an ulcer. The unusual facts are: first, that it has been rather continuous during this time; second, that it is worse on exertion; third,

that it radiates up under the sternum. All of these things may, of course, occur with complicated ulcer. An ulcer which has invaded the peritoneum can cause some perigastritis. It may give a continuous distress or continuous pain instead of an intermittent one. An adherent ulcer, adherent to the surrounding viscera or to the abdominal wall, may cause a pain which is worse on exertion, and finally adhesions to the small intestine or to the gall-bladder may cause a pain which radiates up to the sternum. The cyanosis is very slight, the heart apparently normal, but yet when we have a pain even in the epigastrium which is worse on exertion the heart must be taken into account. A negative physical examination has no significance, as myocarditis, for instance, may be of the most extreme grade, with no enlargement, no murmurs, and no other objective findings, all changes being indicated by functional variations, indicating a limitation of the reserve power of the heart, such as dyspnea on exertion; even the electrocardiograph fails us here.

Before we proceed further it is necessary to consider the meaning of tenderness in the epigastrium. It was formerly believed that tenderness on pressure in this region, especially if limited in area, was very suggestive, if not strictly indicative, of ulcer of the stomach; that is, that such an ulcer was itself sensitive, and that by pressure one could localize the ulcer exactly. Speaking of pain, I pointed out that pain in ulcer was not due to soreness of the raw surface, but that ulcer pains, like pains elsewhere in the gastro-intestinal tract, were due to changes in pressure in the viscera resulting from abnormal peristalsis. One consequence of this might be that the pain could be in the same place, no matter in what part of the stomach the ulcer was situated. Doubt was thrown on the statement that the pain was within the stomach at all by the fact that, in stomachs which were completely dislocated, for instance, in visceroptosis, the pain and tenderness were still felt in the epigastrium. In investigating this inconsistency Raux found that the point of tenderness in ulcer cases and many other stomach cases was directly over the solar plexus, and he believed that the tenderness elicited on deep pressure was the result of pressure not on the ulcer nor even on the stomach,

but on the solar plexus. This interpretation is now discredited, however, as these sympathetic plexuses in other parts of the body are apparently not tender, and there is no reason to believe that nerves because they happen to be transmitting painful sensations should themselves be tender. It is now believed that the tenderness elicited on deep pressure is not within the abdomen at all, but is in the wall of the abdomen, in the skin, muscle, and subperitoneal tissue; that is, in the region of peripheral distribution of cerebrospinal nerves.

The theory is that a painful sensation such as that produced by an increase in intragastric pressure is transmitted probably along the sympathetic nerves to the spinal segment to which these nerves run. These unusual and painful sensations spread to the ending of the cerebrospinal nerve in the same segment, and are by them transmitted to the brain, which then refers the painful sensation to the place from which these sensations most frequently spring, that is, from the abdominal wall and not from the place where they did spring in this particular instance, that is, from the stomach. Such a reaction would have value to the individual. Pain is necessary in order to protect the individual from harm. The stomach has no voluntary protective mechanism, but in the periphery of the body the abdominal walls and the extremities of course have many means of protection, and the reference of pain to them would result in the use of one of these; for instance, stiffening the muscles or using them in other ways. However that may be, the point remains that so far as can be determined by operation, either with local anesthesia or with no anesthetic at all, serious lesions of the gastro-intestinal tract are apparently not sensitive to ordinary painful stimuli, such as burning, pinching, cutting, etc., and that some other explanation must be found for their *apparent* pain-producing powers.

It will be objected that even when no spontaneous pain is felt in the epigastrium of patients who have ulcers of the stomach tenderness may still be elicited on deep pressure. How can this be accounted for if the pain is simply a referred one to the abdominal wall? The explanation given is simple. When a sufficient number of unusual painful stimuli have passed along some sym-

pathetic branch to a certain segment of the cord, a chronic irritable focus is produced at that point of the cord, and the cerebrospinal nerve running from the periphery to that point are, therefore, placed in a state of hyperesthesia, and ordinary pressure on them is felt as pain. This local irritable focus is the explanation of the tenderness which remains after the spontaneous pain has subsided. The reason why it is so difficult to determine the origin of pain in the viscera is evident from this explanation. The sympathetic nerves arise from closely related segments in the cord, and consequently their pains are referred to closely related areas in the skin, and the tenderness is in closely related areas of the subcutaneous tissue. Hence the difficulty in separating them. For instance, the sympathetic nerves that supply the heart probably arise from the upper four dorsal segments; those supplying the stomach from the fifth, sixth, and seventh dorsal segments. The vagus, which also transmits afferent stimuli, extends to the cranial nerve-roots and the upper cervical segments. The liver and gall-bladder are supplied by nerves arising from the seventh to the ninth dorsal segments besides, of course, being innervated by the phrenic, which arises from the upper dorsal segments.

The cerebrospinal nerve supply of the upper epigastrium is from the fifth to the seventh dorsal segment. It is, therefore, easy to see how painful sensations originating in the stomach are almost invariably referred to this region, and how painful sensations arising from the liver and gall-bladder and transmitted to the segment below, and those arising from the heart and transmitted to the segment above, may, if they are violent enough, spread to the sixth and seventh segments and be referred to the region to which ordinarily the gastric sensations are referred.

It goes without saying that the muscular rigidity in uncomplicated gastric ulcer and a sense of constriction occurring so often in connection with heart pains is a muscular contraction or increase in muscle tone, a defense phenomenon which occurs in these referred pains in the same way as it would occur if the pain really was originating in the abdominal wall or in the chest wall, a so-called visceromotor reflex. We must always remember

in this connection that besides the pains referred to the segment of body covering immediately over the viscus, there may be pains referred to much more distant portions of the body, provided that part of the innervation of the viscus is connected with the spinal segment which supplies those portions of the body; for instance, pain in the stomach or, rather, a disturbance in the stomach is sometimes felt as pain in the neck, or in the jaw on the left side, of course, most frequently. This is probably due to the fact that the vagus carries sensory stimuli and proceeds partly from the lower cervical segment, from which also the skin of the neck is supplied. Heart pains are felt on the inner side of the arm and fingers because its sympathetic fibers arise partly from the lower cervical and upper dorsal nerve which supply the skin of the arm.

There is, however, one class of visceral pains which must be separated from the above, as they respond to a different law; that is, the class in which inflammation or growth, that is, malignancy, has extended beyond the limit of the viscus and involves by pressure cerebrospinal nerves in the neighborhood. The pain, then, is felt somewhere along the course of these nerves. For instance, in a carcinoma of the cardia which has extended backward so as to involve an intercostal nerve, the pain may be felt in the lower axillary region. The intercostal muscles here are rendered tense and hyperesthetic. The pain is worse on deep inspiration, and the whole picture resembles a pleurisy quite closely. Carcinomas of the cardia are very difficult of recognition, either from the history, clinical findings, laboratory findings, or the *x*-ray findings. Therefore it should always be thought of when no adequate explanation of the pains in the left lower axillary region can be found.

In the present case, while the history of gastric distress, eructations, and the presence of pain and tenderness in the epigastrium seem to point to a gastric origin, the fact that the pain was worse on exertion or apparently at times originated after exertion made a cardiac origin possible, and, as I have tried to explain, cardiac pain may perfectly well be referred to the epigastrium, especially if intense. The fact that it did not radiate down the arm is, of course, of no importance. We should simply say that

in the present instance it radiated to the *lower* dorsal segment rather than to the *upper* dorsal segment. Owing to the fear that it might be anginal in origin, we made no attempt to pass the stomach-tube, but did examine the gastro-intestinal tract with the *x*-ray.

Fig. 239.—Stomach pushed to right by distended splenic flexure. The curve of the latter is unusually broad, suggesting adhesions to diaphragm.

On fluoroscoping him, before giving him an opaque meal, we were astonished to find that the whole of the gastro-intestinal tract could be outlined clearly by means of the enormous amount of gas therein contained. The whole of the stomach and intestines could be thus easily seen. The cardia was greatly distended with gas, a most unusual condition outside of intestinal obstruction, which, of course, is not present here. When barium was

given the dilated cardia was still more evident, the pars media was pushed over to the right, apparently by the distended splenic flexure (Fig. 239). The duodenum was well filled, but somewhat immobile. The stomach emptied rapidly, the motility being three hours, by which time the barium was in the pelvic ileum. In six hours the barium was in the transverse colon and in twenty-four hours in the descending colon. The splenic flexure seemed

Fig. 240.—Upper arrow points to diaphragmatic adhesions; lower, to broad splenic flexure.

to take a wider bend than the usual acute angle. The lower left chest showed some adhesions, pulling up part of the left half of the diaphragm (Fig. 240). We interpreted this as a remnant of the pneumonia which the patient believes was on the left side. In short, except for the marked meteorism and the possible adhesions of the splenic flexure to the diaphragm, the gastro-intestinal tract was normal, not supplying us any grounds for the diagnosis of gastric ulcer or gastric carcinoma. We have left,

then, the only other possibility, namely, cardiac pains or angina pectoris, and this, I believe, to be the interpretation of this case.

The other doubtful point can be readily explained. The fact that the distress comes on after meals is, of course, a frequent complaint in cardiac weakness. The extra exertion to which the heart is subjected during digestion, possibly a direct pressure from a distended cardia, embarrasses the weakened heart, and may cause dyspnea in one case and cardiac pains in the next. Our patient divides his distress into two kinds: one, an immediate distress which he feels as a sense of constriction in the epigastrium however, not in the precordium. The explanation, however, is surely the same. It is a visceromotor reflex due to heightened tension of the muscles of the abdominal walls and the lower intercostal muscles. One or two hours later he feels the real anginal pain, only, as stated before, in the epigastrium and under the sternum rather than in the arm. The patient himself insists that his distress must be gastric in origin because he is immediately relieved by belching or by passing gas per rectum. This is an interesting point and we shall consider it a little in detail.

Gas in the intestinal tract may arise from two sources: first, from fermentation of carbohydrates and to a less extent from proteins, and, too, from swallowed air. The oxygen from the latter is mostly absorbed in the stomach, part of the nitrogen passing onward into the intestines. Unquestionably, the gas ordinarily found in the stomach is due to swallowed air, there being very little opportunity except in cases of extreme gastric stasis for fermentation. An excess of gas in the intestines may be due to excessive production or, second, to diminished absorption or diminished elimination. For instance, in the aged we may have both of the latter factors present. We may have a marked atrophy of the musculature resulting in a reduced peristalsis; hence a diminished elimination and a proved atrophy of the mucosa probably resulting in a diminished absorption. A combination of these three factors results not infrequently in a fluoroscopic picture such as was seen in the present instance. Here, I believe,

the factor of increased production was also present. It is a fact that in some cases of angina the end of the pain is attended by violent eructations or passage of flatus. The explanation of this phenomenon is that during the intense pain the patient remains quiet, with chest expanded, diaphragm raised, and glottis closed, the whole, of course, being quite involuntary. As a result of this, the pressure in the stomach is lowered and air rushes into the esophagus. The stomach becomes distended, and as soon as the most severe part of the pain is over, the patient eructates and obtains some relief therefrom, and considers that the pain must have been due to the presence of the gas in the stomach. Naturally, he attempts to belch still more, in the meantime unconsciously swallowing more air. The noise of eructation may be quite loud, the whole almost impressing one as an hysteric phenomenon, if it were not for the agony that is evident in the patient's face. It is easy to see how the eructations, coming on after a full meal and accompanied by pain in the epigastrium, lead one occasionally to think seriously of a primary gastric disturbance. While recognizing this factor in our patient, it was thought also that the presence of a slight excess of starch granules and cellulose in the stools might indicate a factor of increased production of gas through fermentation, and this was taken into consideration in the treatment.

In order to test the accuracy of our diagnosis the therapeutic test was applied. The patient was put in bed, a diet was given containing rather high protein and fat, with a minimum of cellulose and carbohydrates, and at the onset of distress $\frac{1}{100}$ gr. of nitroglycerin was given, repeated at ten-minute intervals for four or five doses. The effect was very striking and the attack stopped quite abruptly, most unusually so, according to the patient.

I do not wish to go into detail as to the etiology of angina pectoris. It is a disputed point at present, but I believe that the theory of muscular insufficiency answers clinically most satisfactorily. The theory of coronary sclerosis, or of aortitis plus coronary sclerosis, is not an explanation of all cases of angina, as numbers have been reported in which the necropsy showed no

sclerosis present. The similarity to intermittent claudication of the lower extremities, therefore of muscular exhaustion, is striking. This may result, first, from an insufficient blood-supply, that is to say, a coronary sclerosis, or, too, there may be a normal supply, but a weakened muscle. The result will be the same. The individual may get an attack whenever the muscle is overexerted. He may get an attack, but need not, as the presence or absence of pain evidently depends upon still another factor, perhaps the central nervous system, as it is a notorious fact that we may have the most severe sclerosis of the coronary arteries or the most severe myocarditis and still no angina, while it is not so well known but equally true that we may have severe anginas with mild anatomic lesions. The prognosis, therefore, depends upon various factors, and for this purpose we might perhaps divide anginas into several classes: first, those occurring in the young, under which we may include heart pains arising in an apparently healthy heart due to some acute heart strain, and second, those occurring in the hearts of rheumatics or other endocarditis cases of record.

Second, those occurring between the ages of forty and fifty years, which will include the heart lesions resulting from nephritis and hypertension, the luetic cases developing aortitis, the cases occurring in women at the menopause with slight myocarditis, and some presenile cases; and third, the senile cases.

In general, the prognosis is the most serious in the second class of cases, those developing between forty and fifty years, in which there is a progressive nephritis or hypertension or an intractable lues. The occasional anginas occurring in endocarditis of the young is, of course, very serious. The mildest cases are those which occur in boys who have subjected their hearts to a short period of violent strain, especially in competitive athletics. The following is an example:

A boy of fourteen had been complaining for about a week of a choking sensation in his throat and a pain in the precordium. He had no dyspnea on exertion. On examination his apex was diffuse, beyond the nipple line with some dulness under the sternum, a slight systolic murmur at the apex, and a markedly ac-

centuated second pulmonic. The pulse was regular, and 90. Examination otherwise negative. After a week's rest in bed the heart was in the normal position, the murmur disappeared, and the accentuation of the pulmonic was much less. Unquestionably a case of anginal pain due to training for some skating races which had recently taken place.

Equally favorable is the prognosis in women about the menopause, in whom a lifelong neurasthenia has been accentuated by the climacteric and perhaps by some temporary worry. It is not unusual in these cases to find a systolic blood-pressure of 180 or 190, some pain either in the precordium or limited to the left arm, but no dyspnea on exertion. The proper kind of rest in these cases causes the subjective symptoms to subside. The senile cases are, of course, the most numerous, and average somewhere between the above two classes. In considering their prognosis we must remember, first, that the severity of the case is not necessarily proportionate to the intensity of the pain, for here, as in all disease, the intensity of the pain is partially a function of the sensitiveness of the central nervous system, for in the mild menopause cases mentioned above we may have a very severe pain, with a good prognosis.

There are two ways of ascertaining the outlook in any case: one way is to determine the amount of maximum effort without pain. For instance, if a patient has a severe pain on walking after a full meal, but at other times can walk considerable distances without pain, the prognosis is far more favorable, of course, than if he is unable to walk at any time without pain; and second, we must often await the effect of treatment before deciding the outlook. Luetic cases have occasionally a very good prognosis and respond rapidly to treatment; at other times apparently the damage already done cannot be repaired. In general, it is not fair to the patient to alarm him unnecessarily by invariably giving a poor prognosis in every case of angina, as many of them live in comparative comfort and work reasonably hard for ten, fifteen, and twenty years after the onset of the pain, and in other cases the pain entirely disappears after a varying period.

As an example of the senile type I shall outline the treatment for our patient: First of all he was put at rest. He was not required to remain in bed the whole day, as it was felt that some danger of a hypostatic pneumonia existed, and he was therefore allowed to sit up in a chair one hour in the morning and one hour in the afternoon. This is, of course, the prime requisite in all treatment of angina, namely, rest for the exhausted muscle. As the pains came on after meals, an attempt was made to make the meals smaller and to avoid overloading the stomach mechanically by making them as dry as possible and also concentrated. No fluids at all were given during the meals. No butter was added to the bread. He was required to chew all food thoroughly. The meat was given scraped or chopped. As there was some increased starch in the stool, all the coarsest vegetables—namely, those containing 5 per cent. starch—were eliminated, and peas, carrots, potatoes, etc., were passed through a sieve. Buttermilk was given between meals; the evening meal was very small and was given early, with 5 ounces of warm water given at bedtime. He was given cascara in divided doses during the day, and as he had a tendency to collection of stool in the rectum, he was given 1 pint of warm water as an enema each morning. At the first sign of pain or even of constriction he was requested to call for nitroglycerin, which was administered in $\frac{1}{100}$-grain doses repeatedly until the pain ceased. Besides the nitroglycerin during the attacks he was given sodium nitrite three times a day in 5-grain doses. His smoking was cut down from a large number of cigars to two small cigars a day.

Two other drugs are sometimes of use, digitalis and the caffein group. Digitalis is at times apparently of benefit, but I have seen patients in whom it apparently did harm, probably by overstimulating the muscle. At any rate, it should be given in small doses and the patient carefully observed. Caffein, as citrate or as diuretin, is in general of greater value than digitalis, as in most patients with myocarditis whether they have angina or not. Whether it acts simply as a diuretic or relieves peripheral resistance, or directly effects the heart muscles is an open question.

The patient so far has improved remarkably, having now been free of pain for over a week, and the mildest sense of constriction which occurs at times is relieved by a single nitroglycerin tablet. The outlook, therefore, is fair for continued restricted activity. Knowing, however, that the intensity of the pain in this case must be due to considerable anatomic changes, and not to an oversensitive nervous system, we have warned the family that sudden exitus is not out of the question.

CLINIC OF DR. JULIUS H. HESS

COOK COUNTY HOSPITAL

TUBERCULIN SKIN REACTIONS IN DIAGNOSIS OF TUBERCULOSIS IN CHILDHOOD

CASE I.—This four-year-old boy was admitted August 23d with the history of cough, fever, loss of appetite, and general malaise of eight days' duration. The cough was not productive and he suffered from a moderate degree of dyspnea.

Past History.—Pneumonia two years ago, measles and pertussis eight months ago; has always been of delicate constitution.

His family history is negative.

Physical Findings.—Positive findings: Lessened expansion on right side of thorax, increased vocal and tactile fremitus over whole right chest, and dulness over upper and lower right lobes anteriorly and posteriorly and over middle lobe anteriorly. Distinct bronchial and tubular breathing, with bronchophony and pectoriloquy over right chest. Many crepitant and subcrepitant râles. Temperature 101.6° F., pulse 120, respirations 36.

Laboratory Findings.—Hb. 60 per cent., RBC 5,120,000, WBC 11,600, polymorphonuclear 71 per cent., small mononuclear 20 per cent., large mononuclear 9 per cent. Urine negative. Pirquet positive. Quantitative intradermal test positive with all four injections, quantity of tuberculin used 0.00005 mg., 0.0005 mg., 0.005 mg., and 0.05 mg. (Fig. 241).

Course.—The lung findings persisted with but slight changes until the end of the first week. At that time, the note over the right chest being flat, aspiration was done and about 500 mils. of clear fluid withdrawn. No organisms were found. The child improved gradually, temperature declining by degress to normal. At the end of the third week physical findings in the right lung

were as follows: Dulness present on the right side, from the level of the fourth rib downward. Few fine râles present, but no bronchial breathing. Breath sounds diminished posteriorly, absent laterally and anteriorly.

Roentgenogram.—The picture was taken ten days after admission or three days after pleural cavity was aspirated. There is first seen a spinal curvature to the left, with an increase in size of the left intercostal spaces, and a corresponding decrease in width of the right. The heart is not displaced. The arch of the aorta shows to the left of the spine. The dense shadow in the peribronchial glands suggests an old process followed by calcification of these glands. A distinct vertical line is seen on the right

Fig. 241.—Case I. Positive intradermal quantitative tuberculin test.

side. This is probably the line of separation between the compressed lung and the fluid in the pleural cavity. The shadows over the outer half of the right lung are denser than that of the left, probably because of compression and congestion. The small shadowy dots seen over the compressed portion of the right lung are due to enlargement of the bronchial lymph-glands. Heart outlines about normal (Fig. 242).

Subsequent History.—The child was discharged at the end of a few weeks with all findings improved; there, however, remained an area of marked dulness over the right lower lung posteriorly, and later roentgenograms showed increased hilus and peribronchial shadows, as well as an area of calcification in the right lower lobe.

This represents an advanced case of pulmonary tuberculosis with associated tubercular pleuritis in a child with sufficient antibody formation to cause a marked reaction to the old tuberculin

Fig. 242.—Case I. Pulmonary tuberculosis with pleuritic effusion on the right side.

when administered in performing a cutaneous and an intracutaneous test.

CASE II.—This seven-month-old infant gives a history dating back two and half weeks, when the child fell from a cart, striking his head. Two days following the injury he vomited repeatedly,

became restless, and drowsy. He continued in a stuporous condition for about one week, when he developed a series of convul-

Fig. 243.—Case II. Typical mottling of generalized miliary tuberculosis in both lungs.

sions, followed by an internal strabismus and dysphagia. There is nothing important in his personal history other than that he was a bottle-fed baby since birth.

Family History.—His mother has an active pulmonary tuberculosis. His father and three other children are living and well.

Physical Findings on Admittance.—General appearance that of an apathetic, drowsy child with an internal strabismus, deep sunken eyes, and extreme pallor. Skin is dry, inactive, and shows numerous papulonecrotic tuberculids scattered over the body. Cervical glands are palpable. There is an internal strabismus which is most marked in the right eye. Neck: Brudzinski positive, otherwise negative. Thorax: Marked impairment of resonance associated with bronchial breathing and numerous râles heard throughout both lungs. Abdomen negative except that the liver was palpable two fingerbreadths below the costal arch. Nervous system: Babinski, Gordon, Oppenheim signs, all positive on both sides. Tache cérébrale very markedly positive.

Laboratory Reports.—Urine negative. Blood: Hb. 85 per cent., RBC 4,224,000, WBC 12,600, polymorphonuclears 62 per cent., small mononuclears 29 per cent., large mononuclears 7 per cent., transitional 2 per cent. Spinal fluid examination: Cell count 800, 96 per cent. lymphocytes; Noguchi, Ross Jones, and Nonne positive. Pellicle formation, but no micro-organisms found. Von Pirquet negative on three successive tests. Intracutaneous test of old tuberculin with four injections, the quantity of tuberculin used being 0.00005 mg., 0.0005 mg., 0.005 mg., and 0.05 mg., were all negative.

Roentgenogram showed the typical mottling of generalized miliary tuberculosis in both lungs (Fig. 243).

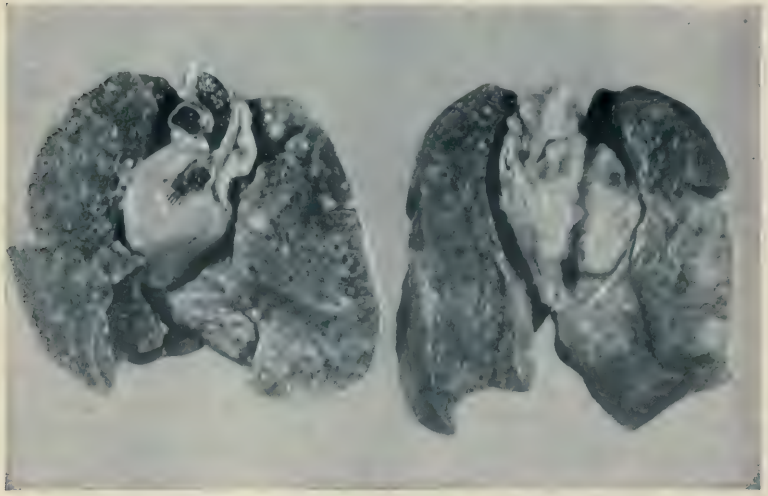
This case represents an advanced type of acute miliary tuberculosis associated with a tubercular meningitis, and a generalized bilateral lung involvement. In an infant so overwhelmed by the infection the cutaneous and intracutaneous tests remained negative even on repeated inoculations.

Subsequent History.—The child died six days later. At autopsy the roentgenograms were confirmed by the finding of generalized miliary tuberculosis (Fig. 244).

The positive value as well as the shortcomings of the various tuberculin reactions are well illustrated by the above cases. While a tentative diagnosis of tuberculosis could be made in Case I,

based on the presence of serous exudate in the pleural cavity following the development of acute pulmonary findings, the positive skin reactions were of definite value. In Case II, in which a positive diagnosis of acute miliary tuberculosis could be made from the spinal fluid and the roentgenogram, the skin reaction remained negative due to the overwhelming infection.

In the following we will, therefore, attempt a more careful study of the conditions necessary to positive skin reactions, dis-



Postero-anterior view through middle of lung. Postero-anterior view of posterior surface of lung.

Fig. 244.—Case II. General miliary tuberculosis and tuberculous meningitis. Shows primary lesion and secondary glands. Skin tuberculides.

cuss the history of the skin reactions, the nature of tuberculin reaction and its technic, describe the typical reaction and various types, the modification of original Pirquet technic, quantitative tuberculin tests, differential tuberculin tests, intracutaneous tuberculin test, subcutaneous test, the histopathology of tuberculin papule, inquire into the specificity of tuberculin skin reactions, define the meaning of positive and negative tuberculin skin reactions, and estimate its value in diagnosis and prognosis.

The skin is one of the tissues of the body which readily reacts to influences from within or without. There are two factors which are absolutely essential for the production of a skin reaction. There must be an agent capable of acting on the skin, and the skin, in turn, must be of sufficient vitality to be able to react to this agent. The ability of the skin to react is a matter of great importance. The character of the reaction produced is, however, dependent upon different conditions. The reactivity of the skin may be lowered with the lowered vitality of the body, as in markedly cachectic individuals, or it may be entirely absent in such cases. Newborn infants and infants in the first year of life frequently do not show any reactivity to certain noxæ, because the cells of the skin have not yet acquired the power of reaction (Moro[1]). In such instances the reaction is either very feeble or the skin is entirely unresponsive even to agents which otherwise are able to produce a reaction. A hypersensitiveness of the skin, on the other hand, may increase the reactivity to such an extent that an excessive reaction is produced to certain noxæ and even to agents that under normal conditions would be innocuous and ineffectual. This hypersensitiveness of the skin, which may be either "an inherited cutaneous irritability" or be present "in those of an active nervous temperament or in gouty and rheumatic subjects," is also regarded as an important etiologic factor in the production of the so-called eczematous skin reactions to agents which under normal conditions would provoke no reaction at all or a very mild reaction (Stellwagon,[2] Combe[3]). This may probably be an explanation of the results obtained by Schmidt[4] while investigating the action of different food substances applied to the skin in the same manner as the Pirquet test. His results showed a positive reaction in 40 per cent. of the cases, similar in character to the positive Pirquet reaction. The tests were made on 100 children suffering from different diseases, and it is interesting to note that the largest number of positive reactions was obtained in the cases of functional neuroses and arthritic diatheses, which corresponds to Stellwagon's observations on "those of active nervous temperament and gouty and rheumatic subjects." The reactivity of the skin is of great significance in test-

ing the specificity of the cutaneous tuberculin tests and also in interpreting positive and especially negative results. We shall have occasion to discuss it more fully later.

The character of the skin reaction varies from simple temporary hyperemia to structural changes, such as the production of papules, vesicles, pustules, etc. Structural changes of the skin generally result from excessive action of agents which when mild would produce but temporary hyperemia (excessive pressure, friction, excessive heat, overdoses or systemic accumulations of some drugs), or from the action of agents which in themselves are injurious to the skin or become injurious due to changes which have been produced in body fluids by previous existence of some disease.

Cutaneous reaction with formation of papule may be obtained by injection of chemical substances, complex poisons of bacterial origin, known as toxins, as those of diphtheria, typhoid, typhus, pyocyaneus, etc. (Entz[5]). All these toxins are primarily poisonous, that is, poisonous and injurious, therefore causing skin reaction in normal subjects. And yet in some cases no reaction may be obtained on injection of diphtheria toxin. This is explained by assuming that the toxin is destroyed by specific antibodies before it can act upon the skin and cause it to react in turn. It is this principle that has been made the basis of the Schick test. On the other hand, there are toxins that are only secondarily poisonous, that is, they are in themselves non-poisonous in normal individuals, but they become poisonous and capable of provoking skin reactions in individuals in whom some changes in the body fluids have taken place as the result of the previous existence of some diseases. Tuberculin, emulsion of Bacillus tuberculosis and their toxins are examples of this class (Hamburger[6]).

History.—The first man to call attention to skin reactions, as far as is known, was Edward Jenner,[7] who in 1798 described an "efflorescence" of a palish color at the site of injection of variolous material in a woman who had cowpox thirty-one years before. The next man to describe a skin reaction was Robert Koch,[8] who in 1898 showed that a single injection of living tubercle bacilli under the skin of the guinea-pig produced an ulcer, then

an infected gland, and finally a generalized tuberculosis, but that repeated injections produced a much more violent local reaction, ending in necrosis with an absence of the generalized infection.

In 1903 Arthus[9] described the local phenomenon of anaphylaxis in rabbits, as being manifested by redness, swelling, and wheal formation, and a local sloughing of tissues at the site of repeated hypodermic injections of horse-serum. This has been called the Arthus phenomenon of anaphylaxis, and is contrasted from the general anaphylactic reaction seen in its extreme form in a guinea-pig, and known as the Theobald Smith phenomenon.

Skin reactions as a diagnostic measure, however, have first been described by von Pirquet in 1908,[10] who made use of Koch's tuberculin by applying it on the skin and abrading the skin with a scarifier made for that purpose. He was followed by other men who used different methods, but applied the same principle for the diagnosis of tuberculosis (Calmette, Mantoux, Wolf-Eisner, and Moro).

The tuberculin skin reaction was followed by other skin reactions applied for the diagnosis of other diseases. In 1908 Schick[11] described a cutaneous reaction for diphtheria. In 1911 Noguchi[12] described a cutaneous reaction in syphilis. In 1912 Irons and Nicols[13] described a skin reaction for gonococcus infection, and in the same year Schloss[14] described an anaphylactic food reaction, especially one due to egg albumen. The above-named reactions have been standardized and used extensively for diagnostic purposes. In addition to the above, numerous other skin reactions have been described; for instance, a reaction for strepthothrix, for typhoid, for varicella, and for hay-fever, and other articles used as foods. The latter, however, have not been standardized as yet and their specificity is still in doubt.

The most widely used skin reaction is, beyond doubt, the tuberculin reaction, of which the Pirquet method is the one most frequently employed.

Nature of Tuberculin Reaction.—According to Pirquet[15] the tuberculin reaction is due to the fact that the tuberculin be-

comes digested by specific antibodies at the place of application. These bodies have been formed by the organism because of a preceding infection by tuberculosis, and they are present in all the fluids and all tissues of the body. The test is, therefore, an allergic reaction, that is, it shows a change in the condition of tissues or, in other words, the organism which reacts to local application of tuberculin by formation of a papule possesses a hypersusceptibility toward toxins and metabolic products of tubercle bacilli which was acquired by a preceding tuberculous infection.

Wolff-Eisner's[16] idea of the reaction is that the lysins of the body of a tuberculous individual produce special bodies by destruction of tubercle bacilli.

Moro[17] thinks that the tuberculin reaction is a specific nervous allergia which is manifested by a local angioneurotic inflammation.

Technic.—Tuberculin tests are divided into qualitative and quantitative. The simplest of the qualitative tests is the von Pirquet test.

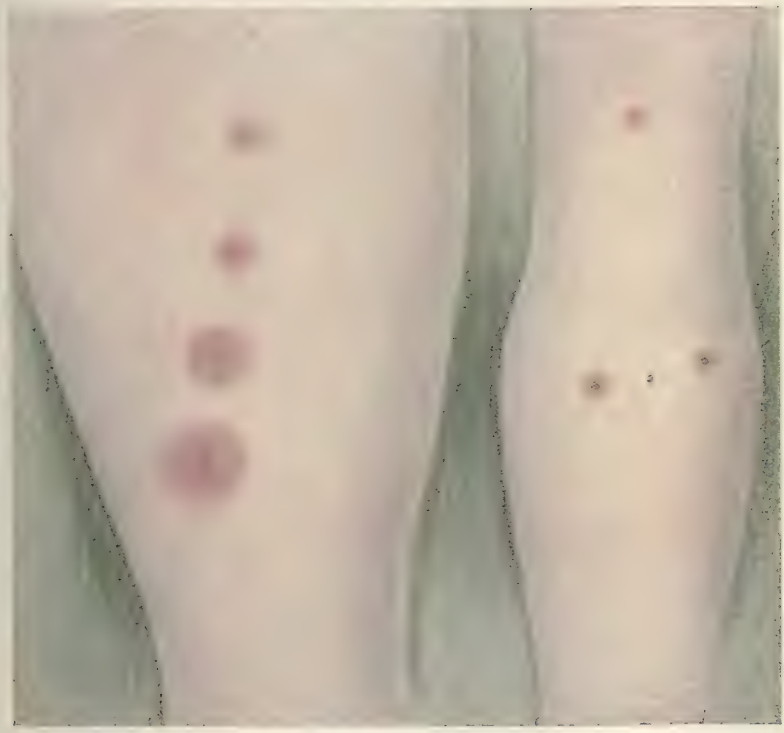
The skin is cleansed with alcohol or ether and 2 drops of tuberculin applied about 5 cm. apart. With a suitable instrument, preferably a platinum-pointed borer, a superficial abrasion is made in the skin between the two drops, and then a similar abrasion is made through each drop of tuberculin. Two drops of tuberculin are used to judge the uniformity of the technic, the abrasion without tuberculin as control.

No dressing of any character is required.

The tests are inspected at the end of twenty-four hours and the points where tuberculin was applied carefully compared with the control abrasion and, where possible, again at the end of forty-eight hours; when only one inspection is possible, forty-eight hours is preferable.

Reaction.—The reaction is positive when a papule forms which is visible and palpable for several days. The control shows the so-called traumatic reaction, which consists of a swelling with rose-colored areola, which shows after several hours a scab with red margins.

PLATE 3



A *B*

A, Quantitative intradermal tuberculin reaction. Reading from above down: 1, Control; 2, 1/20000 mg.; 3, 1/2000 mg.; 4, 1/200 mg.; 5, 1/20 mg. Salt solution is used for the control and old tuberculin for the tests.

B, Test on forearm: Von Pirquet cutaneous tuberculin test (positive reaction, showing two positive reactions and control in center following the application of full-strength old tuberculin). Test on arm: Mantoux intradermal tuberculin reaction following the intradermal injection of 1/2000 mg. of old tuberculin.

The reactions are usually designated as follows:

1. Negative reaction; no appreciable difference between the tuberculin areas and control.

2. Slight reaction; definite, but slight redness with some infiltration.

3. + reaction; wider area of redness, with a definitely raised center.

4. ++ reaction; wider areas of redness, with more marked infiltration than +.

5. +++ reaction; unusual redness and wide area of infiltration including all cases which go on to vesiculation.

Types of Reaction.—1. The *usual* or *typical* tuberculin reaction begins to appear in from four to six hours, reaches its maximum in from twenty-four to forty-eight hours, and then rapidly fades, although the infiltration may persist for several days.

2. The *premature* reaction is characterized by a rapid course and slight intensity. It begins in from four to six hours, reaches its maximum speedily, sometimes after only ten hours, and disappears rapidly, not later than on the second day. This type is supposed to occur in patients with manifest tuberculosis who are not doing well.

3. The *persistent* reaction begins like the others, but reaches its maximum slowly and gradually, usually at the end of the second day, and in some cases still later, the maximum persisting unchanged for a week, and often for two or three weeks.

4. The *late* reaction makes its appearance after an incubation period of over twenty-four hours, and develops and recedes slowly. The third and fourth of these types are supposed to occur in patients with inactive lesions.

5. The *cachectic* reaction is characterized by infiltration with little or no redness. It can be better appreciated by touch than sight. This type, as the name indicates, is common in late stages of tuberculosis.

6. The *scrofulous* reaction: One or more papules are present and they are surrounded by a painful area of redness often 5–10 cm. in diameter. This type of reaction is seen in children suffer-

ing from exudative diathesis and is seldom seen in adults (Combe, *loc. cit.*).

In a proper study of the reaction the record should show the diameter of the lesion, the intensity of the redness, the amount of infiltration, the size of the central papule, and in older children the amount of pain.

Modifications.—Numerous modifications of the original von Pirquet test have been proposed. In general, these modifications may be arranged into two groups: 1. Those in which the technic is modified in order to make the reaction more reliable and the results more uniform. 2. Those in which the technic has been modified in order to make the diagnosis more specific as far as the activity of the disease is concerned, or in respect to the specific bacillus (human or bovine) causing the disease.

Aside from intracutaneous and subcutaneous tuberculin tests, which will be discussed later, the majority of the modifications of the first group comprise minor changes in the technic. One modification, however, that of Lautier, makes a fundamental change in the test in not scarifying the skin at all and applying 1 per cent. solution of old tuberculin on a pledget of cotton, directly to the skin. Lyman,[18] however, who has studied this reaction and compared it with that of von Pirquet, comes to the conclusion that it is very doubtful whether the Lautier test has any value at all.

Quantitative Tests.—Attempts have been made to perform quantitative cutaneous tuberculin tests in order to be able to judge as to the severity of the disease, whether active or in latent stage, but the results have shown that all these tests have little if any practical value. Ellermann, Erlandsen, and Peterson[19 20] have brought the technic of these tests to their highest perfection. They have standardized their technic by using tuberculin of definite dilution and by measuring the extent of skin scarification. After the papules appear, they measure them very carefully and, taking an average from these figures, they calculate the degree of the sensitiveness of the individual. With all these refinements of technic one of their conclusions as to the value of these tests is that "there are so many individual variations in each group

(clinically non-tuberculous group, clinically tuberculosis suspected group and definite tuberculosis group), that one cannot diagnose tuberculous disease from the tuberculin titer alone. However, in conjunction with the general clinical symptoms it is a valuable indication. Hamman and Wollman[21] regard it as possessing very little if any practical value, since "exact mathematical calculations are applied to factors of indeterminable variation," and because "the cutaneous test is a relatively rough one and utterly unsuited for quantitative tuberculin tests. Intracutaneous tests alone should be employed in determining the degree of hypersensitiveness."

Differential Tests.—Differential cutaneous tests have been made for the purpose of differentiating between tuberculosis caused by Bacillus tuberculosis hominis and Bacillus tuberculosis bovis. Detre's[22] differential cutaneous reaction consists of performing the von Pirquet test by the simultaneous application, in series, of human old tuberculin and of human and bovine bouillon filtrates. Measuring the resulting reaction in millimeters, he believes himself able to draw reliable conclusions as to whether the patient has been infected with the bacillus of the human or bovine type, and as to whether the disease at the time of the test is active or latent. Several other observers (von Pirquet,[23] Schütz and Vidéky,[24] Hamman and Wollman, *loc. cit.*) report that this method is of no value and is not reliable and not practical.

Cuttaneo[25] reviews the discussions as to the identity of human and bovine tuberculosis and gives his own results in a series of 45 cases of tuberculosis in children treated with both human and bovine strains of tubercle bacilli. He found that some cases of bone, bowel, and gland tuberculosis reacted much more frequently and readily to bovine tuberculin, while, on the contrary, a larger percentage of pulmonary cases reacted to the human form.

H. Nothmann[26] vaccinated a number of children with human and bovine tuberculin. He wished to see whether it could be ascertained in this way which is the infecting organism; 207 children from one to sixteen years of age were tested. From these

56, or 27 per cent., did not react to either. In 145 the test was positive, and in 133, or 91.7 per cent., of these it was positive to both tuberculins; in 2, or 1.4 per cent., to bovine alone, in 9, or 6.2 per cent., to human alone. Nothmann thinks that this method is of no value in determining the variety of the infecting organism. He thinks that only one fact can be gleaned from these observations, that the majority of tuberculous patients react both to human and bovine bodies, and that the homologous group is stronger than the specific group. Therefore, no matter what the variety of infection, a double reaction occurs.

Several other observers report that this method is of no use and is not reliable. This has also been our experience in a large series of cases in which the test was performed simultaneously with human and bovine tuberculins. In most instances both were either negative or positive, and in the latter the reaction was of equal intensity in most cases.

Moro's tuberculin test, in which tuberculin is incorporated in an ointment and the latter then applied with friction to the unbroken skin, has been proposed as a modification of the original Pirquet test, but this test possesses no advantages over the Pirquet test.

Intracutaneous Tuberculin Test.—Although Mendel first suggested intracutaneous use of tuberculin, it is to Mantoux[27] that we are indebted for its practical application. He employed 1 : 10,000 dilution of old tuberculin, and injected $\frac{1}{20}$ c.c. of this solution, thereby administering 0.005 mg.

Hamman and Wollman have modified his technic to the extent of using increasing dosage of tuberculin, making four simultaneous injections of increasing strength. They describe the technic as follows:

"We make four simultaneous injections. The first consists of $\frac{1}{20}$ c.c. of pure salt solution as control; the second of $\frac{1}{20}$ c.c. of 1 : 1,000,000 dilution of old tuberculin, equals 0.00005 mg.; the third of $\frac{1}{20}$ c.c. of a 1 : 100,000 dilution of old tuberculin, equals 0.0005 mg.; the fourth, of $\frac{1}{20}$ c.c. of a 1 : 10,000 dilution of old tuberculin, equals 0.005 mg. If none of the areas react, we may perform a second test upon the opposite arm, injecting $\frac{1}{20}$ c.c.

of 1 : 1000 dilution of old tuberculin, equals 0.05 mg., and $\frac{1}{20}$ c.c. of 1 : 100 dilution of old tuberculin, equals 0.5 mg. In this way a more accurate estimate of the degree of hypersensitiveness is obtained than from a single injection."

In our own work we have used $\frac{1}{20}$ mil. of the third dilution, thereby administering $\frac{1}{20}$ mg. of tuberculin as a ward routine, frequently making use of the serial dilutions in studies where it was thought that information as to the degree of hypersensitiveness would be of value. But we have been unable to draw any definite conclusions as to the prognostic value of this latter method.

In performing intracutaneous tuberculin tests the skin is put on the stretch and the needle introduced very superficially, almost parallel to the surface, so that its point remains in the epidermis. Then inject $\frac{1}{20}$ mil. of the solution, which will form a small vesicle in the skin if the injection was properly made.

When the reaction is positive, an infiltration of white or pink color appears in several hours. It increases during the first twenty-four hours, attaining its maximum on the second day. The nature of the infiltration at that time is of rose or pink color, occasionally pale, edematous. Exceptionally in its center several purpuric points may be seen. Around the entire region of infiltration a halo of rosy erythema develops. Occasionally an intermediary zone separates the central nodule from the peripheral halo.

The place of infiltration is rarely smaller than 1 cm., frequently larger than 2 cm.

The reaction begins to retrogress the second or third day. The peripheral halo disappears first. The central nodule takes on a violet tinge, later brownish, and is being gradually absorbed.

Atypical reactions are extremely rare, and they are observed chiefly in cachectic individuals. They are usually slow in their appearance, appearing on the second day and attaining their maximum on the third day. They must be differentiated from pseudoreactions, which are only the result of the injury done to the skin during the test.

As a possible source of error in performing this test it has been pointed out that certain diseases may possess an extreme sensi-

tiveness to tuberculin. Mantoux found, however, that the individuals who did not react to an injection of $\frac{1}{100}$, did not give intradermal positive reactions even when the dose was fifty times as much.

The intracutaneous test is more sensitive than the cutaneous test of von Pirquet. In our experiments, whenever the cutaneous test was positive the intradermal test was also positive in all cases, and, besides that, the intradermal reaction was positive in many cases where the cutaneous reaction was negative. But not even by this more delicate test is it possible to differentiate between infection with human type and that with bovine type of Bacillus tuberculosis.

There are four advantages of the intradermal test over the cutaneous test of von Pirquet:

1. More exact dosage.
2. Earlier reaction.
3. More distinct reaction.
4. More reliable, because of the certainty of absorption.

Subcutaneous Test.—Hamburger depot reaction or subcutaneous tuberculin test has also been recommended for the diagnosis of tuberculosis. It appears, when positive, in ten to twenty-four hours as swelling of subcutaneous tissue in the place of injection, the swelling being 20 to 70 mm. in diameter, and is often but not constantly associated with reddening of the overlying epidermis. Often when no reddening is present and the reaction in general is mild, it may better be palpated than seen. In case of uncertainty it is advisable to palpate at the same place on the opposite side.

In order of their sensitiveness the various cutaneous tuberculin tests may be arranged as follows:

1. Intracutaneous test.
2. Subcutaneous local test.
3. Cutaneous test.
4. Percutaneous test.

This relation is definite, but not absolutely constant.

Histopathology.—The structure of the papule which occurs

in positive cutaneous tuberculin test points to its origin through a histologic reaction of a specific kind. Bandelier and Kreibich,[28] Daels,[29] and La Page,[30] who have made microscopic examinations of the papule, found changes identical with the specific structure of tubercular tissue or of tubercle itself.

Specificity.—Much discussion and a large amount of clinical, postmortem, laboratory, and experimental studies have been done on the question of specificity of the cutaneous tuberculin tests. There are two questions which must be considered and definitely answered before deciding the question of the specificity of the cutaneous tuberculin tests:

1. Does the tuberculin papule occur in tuberculous individuals only? Or a modification of this question: Does the tuberculin papule ever occur in a non-tuberculous individual?

2. Does the tuberculin papule occur in all tuberculous individuals? Or a modification of this question: Is the tuberculin papule ever absent in a tuberculous individual?

In answering these questions it is to be kept in mind that the cutaneous tuberculin test is a practical test, and that, therefore, it is sufficient to prove its practical specificity, to prove its specificity in practical terms, or in other words, to prove that it is specific under the usual conditions of its technic and its interpretation. This relieves us of the duty of proving that the production of tuberculin papule is absolutely specific, that is, that there is no other substance with which we can artificially produce a tuberculin papule; but even this absolute specificity seems to be highly probable if we apply as criterion histologic structure of the papule. Thus, it is not necessary to discuss either the report of Entz,[31] who found that the formation of papules identical (macroscopically) with those seen after tuberculin tests may be produced by other toxins (diphtheria, typhus, paratyphus, pyocyaneus) in about the same percentage of cases, or conclusions of Tezner,[32] who states that the Pirquet reaction is not absolutely specific, but that it is a sign of a somewhat more general allergia, most probably an increased reactive ability against proteins of all bacteria with which the organism is infected at the time at which the reaction is performed, but that from a clinical point of

view, however, the Pirquet reaction remains specific not for the toxin, but for the infected.

Kasahara[33] has made histologic examinations of the papules produced by vaccinating with tuberculin, diphtheria toxin, and atoxyl. Macroscopically, these skin reactions are very similar, but histologically Kasahara found decided differences. The papule resulting from the tuberculin test showed giant cells and infiltration of lymphocytes around the blood-vessels. The giant cells were due to irritation by the tuberculin. The diphtheria toxin papules showed decided changes in the vessel walls. There was thickening of the intima, dilatation and engorgement of the vessels, and a fibrinous inflammation of the corium. The atoxyl papule showed a somewhat marked lymphatic infiltration into the corium. Kasahara thinks that this histologic study is proof that the tuberculin reaction is a specific one.

In discussing the specificity of the cutaneous tuberculin test three things must be kept in mind constantly: 1. What is a tuberculin papule? 2. Who is considered as a tuberculous individual? 3. Conditions of the skin necessary for the production of any reaction.

A tuberculin papule is a papule occurring after cutaneous administration of tuberculin and having histologic structure of a tubercle. For practical purposes its macroscopic characteristic, as previously described, and the fact that the place where control scarification was made shows no papule, are usually sufficient to regard a papule as a tuberculin papule.

As tuberculous individuals are to be regarded not only those that show at present clinical evidence of tuberculous disease, but also those clinically healthy individuals, who have either a latent or a healed tuberculous focus, having been at some time infected with Bacillus tuberculosis. Clinical findings of tuberculosis are sufficient in many cases to regard an individual as tuberculous; absence of clinical findings, however, is not sufficient to exclude the diagnosis of tuberculosis. The best criterion for deciding this question is an autopsy, but in this also it is the positive result that is of absolute value, the negative results having a relative value only. Ghon,[34] in his description of 747 autopsies in children,

found 184 cases of tuberculosis, and in 95 per cent. of the latter cases was able to demonstrate the primary lesion in the tissues of the lungs. He believes that the cutaneous reaction is specific for tuberculosis and that without the positive tuberculin reaction he might easily have discontinued his search for the primary lesion in several autopsies because of his failure to find it upon superficial anatomic examination. However, in all of his cases except 2 he was able to demonstrate tuberculosis, and in these latter 2 cases in which the reaction was positive, but in which he was not able to demonstrate a tuberculous lesion, he is inclined to believe that this was due to his inability to find them and not to an absence of tuberculous infection. Et Shang,[35] in autopsies on 210 subjects, found tuberculosis in 94 per cent. of all cases, and 61 per cent. of these presented no symptoms of tuberculosis during life.

The following table shows the relation between the positive cutaneous tuberculin test and the result of autopsies in these cases.

Observer.	Number of positive reactions.	Tuberculous lesions found at autopsy in—	Percentage of positive cutaneous reactions confirmed by autopsies.
Ganghofner[36]	15	14	93
Müller[37]	22	22	100
Ruck[38]	240	229	95
Total	277	265	Average.. 96

Thus in 96 per cent. of these cases the cutaneous test was absolutely confirmed at autopsy; the remaining 4 per cent. may probably be charged to the inability of finding tuberculous lesions, although they were present.

Pirquet[39] had one case which gave a positive reaction, and in this child no tuberculosis was found at autopsy, but signs of exudative diathesis (Escherich's lymphatismus). Pirquet explains it by saying that there is a very close relationship between lymphatism and tuberculosis and that lymphatism is probably a latent tuberculosis.

We have studied a series of 15 children suffering with exuda-

tive diathesis in whom only 6 reacted to the cutaneous test, which leads us to believe that children, at least in greater part, who are non-tuberculous do not react even though they are suffering with exudative diathesis. In the 6 cases who did react, it was very intensive, the large infiltrated area existing for a much longer time than that of the ordinary reaction. This was especially true in cases suffering from involvement of the mucous membranes and those with phlyctenular keratitis and with marked glandular involvement, which were undoubted cases of tuberculosis. It is our belief that the cutaneous reaction is, therefore, of considerable value in distinguishing the simple cases of exudative diathesis from cases of exudative diathesis with secondary tuberculous infection.

Next, the question is to be discussed whether tuberculin papule occurs in all individuals diagnosed as tuberculous on the basis of either autopsy or clinical findings, other than cutaneous test.

The cutaneous test is not positive in all tuberculous individuals. It may be negative in a number of conditions associated with tuberculosis and in some uncomplicated cases of tuberculosis, especially when the disease is severe.

The conditions associated with tuberculosis in which cutaneous tuberculin reaction may be negative, and often is negative, but usually temporarily only, are:

1. Acute infectious disease, especially exanthematous fevers: Measles (always absent), scarlatina (absent in exanthematous stage), typhus abdominalis, erysipelas. Sensitiveness is markedly diminished or may be absent in pneumonia, diphtheria, and acute articular rheumatism.

2. During pregnancy the positive results of the cutaneous reaction diminish by 50 per cent., and the decrease becomes especially marked after the sixth month.

3. After the introduction of larger doses of tuberculin, as is done for therapeutic purposes. The susceptibility, however, returns afterward.

4. Cachexia from any cause by producing loss of general reactivity of the skin.

5. The following forms of tuberculous disease: Miliary, meningitis, peritonitis, advanced tuberculosis. Some cases of healed and encapsulated, inactive tuberculous foci. Very low reactive capacity of the skin.

In our own experience in making the cutaneous tuberculin test on 630 children we had 15 negative reactions when the clinical diagnosis of tuberculosis was readily made by means other than cutaneous tuberculin test. They were as follows:

Tubercular meningitis, 10.

Marked pleurisy, 2.

Advanced pulmonary tuberculosis, 2.

Severe tuberculosis of hip-joint, 1.

In the cases in which cutaneous tuberculin reaction may be negative even in the presence of tuberculosis we have had the following results:

	Positive.	Slight.	Negative.
Pulmonary tuberculosis	5	2	2
Tubercular meningitis	2	0	10
Tubercular peritonitis	1	4	0
Miliary tuberculosis	2	0	0
Tubercular pleurisy	2	0	2
Tuberculous joint disease	2	0	1

If, therefore, after exclusion of the above enumerated conditions, which may readily be diagnosed by usual clinical methods, we find cutaneous tuberculin reaction positive, we may make a diagnosis of tuberculous infection, which is certain for all practical purposes at least.

Blümel[15] comes to the following conclusions in regard to the specificity of the cutaneous tuberculin reaction: "The cutaneous tuberculin reaction is specific, its presence indicating that the individual is tuberculous, although the disease may be in its healed stage. The specificity of the reaction is proved also by autopsies in many cases. The local changes at the place of inoculation, that is, the papule, corresponds in its minute structure to the structure of a tubercle. By histologic examination it is found that regular tubercle develops made up of epithelioid and giant cells, as well as of the cells of Langhans' type. These structures are not formed by the action of tuberculin *per se*, since

tuberculin is primarily non-toxic, but only in individuals who have been infected previously by tuberculosis the reaction appears."

Meaning of Positive Reaction.—Positive Pirquet test gives indication of present or previous tuberculous infection, and not necessarily of active tuberculous disease.

The quality of the reaction is also of little importance for diagnosis of the intensity of the process, although intensive reaction with the first test means that recently something has occurred; the process may, however, be progressive or retrogressive and of diagnostic value only when clinical findings are considered; however, it may be stated that the younger the patient, the more the likelihood of an active process.

The time of appearance of the reaction is of importance for the diagnosis. Weak positive reactions occur as follows:

1. In an organism once infected, but not now at the height of the infection.
2. May occur in active pulmonary lesions, especially in adults.
3. Miliary tuberculosis and meningitis late in diseases.
4. During or following acute infectious diseases.
5. Previous treatment with tuberculin with overpowering doses.

In children up to two years of age, in whom inactive foci of tuberculosis are extremely rare, the positive Pirquet reaction usually means:

1. Active tuberculosis.
2. It is very often the first sign of tuberculosis at a time when clinical diagnosis of tuberculosis is not possible by any other method.

Meaning of Negative Reaction.—Negative reaction to Pirquet cutaneous tuberculin test, especially if made twice, occurs only in individuals entirely free from tuberculosis, and in definite exceptions, as stated previously.

Diagnostic Value.—The chief value of the von Pirquet reaction lies in its importance for the diagnosis of tuberculosis in infants and young children. Positive reaction is of considerable value in diagnosis during the first year of life, of less during the

second year, of little in childhood, and none in the adult life. On the other hand, a negative reaction excluded, with definite exceptions, the presence of tuberculous lesion. There are, however, certain limitations in the interpretation of the test which are worthy of mentioning. The cutaneous test is not a reliable diagnosticum in itself; it must rather be regarded as a help in clinical examination and observation. These latter ones must always give the answer to the question: Is the present case one that needs treatment or not? The cutaneous tuberculin test cannot, therefore, be used to determine whether a surgical disease of bone or joint is of tuberculous origin or not. It is a mistake to attribute to tuberculosis anomalous auscultatory findings in apices of the lungs because the Pirquet test was positive. Topical diagnosis is not possible by the cutaneous test except possibly in children up to two years of age, in whom inactive foci of tuberculosis are extremely rare. At that age the test is valuable for diagnosis of tuberculosis of lymphatic glands. It is also very good for differential diagnosis between tuberculosis and marasmus, anemia, bronchitis, glandular swellings, cutaneous and bone affections, as well as in beginning meningitis in children up to two years of age.

Scrofulosis gives positive cutaneous reaction without exception. This shows the presence of tuberculous infection, which is usually benign, being manifested by lesions in glands and bones, and only exceptionally leading to pulmonary or miliary tuberculosis.

Exudative diathesis and *lymphatismus* which otherwise can be separated, but with great difficulty, from scrofulosis, can easily be differentiated by Pirquet test. Scrofulosis is today designated as tuberculosis of the lymphatic child, and it can be assumed that the symbiosis of tuberculosis with lymphatism makes the course of tuberculosis milder (Blümel, *loc. cit.*).

Phlyctenulæ give positive cutaneous reaction in over 70 per cent. of cases. In cases diagnosed as phlyctenular keratitis that did not react to the Pirquet test, exudative diathesis has often been determined either from the history or by clinical examination, so that in these tuberculosis-free cases the exudative diathesis has been looked upon as a factor in etiology of eye findings.

The authors question the diagnosis of phlyctenular keratitis in non-tubercular individuals.

Orthotic albuminuria gives very frequently a positive cutaneous reaction, so that one is inclined to bring this disease into connection with tuberculosis, and to regard the orthotic albuminuria as an early symptom of tuberculosis (Blümel, *loc. cit.*).

Pirquet reaction is of no value in choosing wet-nurses (Paten[40]).

Prognosis.—As in diagnosis, the test ought to be only supplementary for prognosis, which is to be made primarily on clinical findings. The Pirquet reaction, no matter how intensive, does not give any indication for prognosis except in infancy, where the prognosis is unfavorable. The negative outcome of reaction in a case of manifest tuberculosis is an unfavorable sign for prognosis. This is true in many cases, but not in all. Cohn[41] found that out of 18 children infected with tuberculosis in the first year of life, 16 died, and in 2 cases only generalized tuberculosis did not occur during the time of observation extending over one year and six months.

Positive test means: 1. In infants, developing tuberculosis and a grave prognosis. 2. In older children, beginning with the second year of life and in adults, it indicates presence of a tuberculous focus in the body, or it is a sign that the individual has been sensitized by tubercle bacilli at some time previous to the test.

Negative intradermal test does not exclude tuberculosis. In the first place, the infection may be recent and the individual may not have had time to produce sufficient antibodies to cause reaction. Where this is suspected, the test should be repeated every month for at least three months. Again, it may be negative because of absence of sufficient antibodies necessary to a positive reaction, either due to overwhelming infection or to some other causes, as have been previously enumerated.

It is interesting to study the frequency of the positive von Pirquet tuberculin reaction in different ages. While the percentages given by different authors vary, all agree that the percentage of positive tests steadily increases during infancy and childhood, to reach a very high figure during the adult life. In the very old

the frequency of the positive results becomes again less than during the adult life.

Paten (*loc. cit.*) performed the Pirquet test on 53 children in ages from one to fourteen days and four infants in the third and fourth week. The result was that not a single child showed even a trace of reaction. All the mothers of these infants except 2 primiparæ showed a positive reaction which, however, in most of the cases was very slight.

On the other hand, Moro[42] states that young infants would not react to the Pirquet test even if they had tuberculosis. The reason for this is probably the fact that the cells of the skin at this time are not yet sufficiently able to form antibodies.

Very few cases of positive cutaneous tuberculin reaction have been reported in children below three months of age.

Müller[43] performed the cutaneous tuberculin test on 160 children up to the age of three months, and found that 13 of them reacted positively, that is, 8 per cent.

A number of other observers could never find positive cutaneous reaction in infants under three months of age—*e. g.*, Sperk (159 cases), Faludi (195 newborn), von Pirquet, Ganghofner (10 cases). L. Cohn (*loc. cit.*) states that below the third month the reaction is always negative.

In a series of 630 children up to fifteen years of age we have obtained positive reaction in 55 cases, and slightly positive reactions in 27 cases. There were 50 cases under three months of age, and of these we have obtained one positive and one slightly positive reaction.

Von Pirquet performed the cutaneous tuberculin test on 988 children and obtained the following percentage of positive reactions:

Age.	Per cent.
0 to 3 months	0
3 to 6 months	5
6 to 12 months	16
1 to 2 years	24
2 to 4 years	37
4 to 6 years	53
6 to 10 years	57
10 to 14 years	68
Over 14 years	90

In our 630 cases in Michael Reese Hospital in whom the cutaneous tuberculin reaction was made, we obtained the following percentages of positive reactions:

Age.	Per cent.
0 to 3 months	2
3 to 6 months	5
6 to 12 months	4
1 to 2 years	8
2 to 3 years	2
3 to 4 years	8
4 to 6 years	15
6 to 10 years	17
10 to 15 years	10

Even if we include among the positive cases our slightly positive cases, then the results in percentage, although getting nearer to the von Pirquet figures, yet remain, on the whole, considerably below those given by von Pirquet, and we get the following table:

Age.	Per cent.
0 to 3 months	3
3 to 6 months	7
6 to 12 months	9
1 to 2 years	11
2 to 3 years	28
3 to 4 years	16
4 to 6 years	19
6 to 10 years	22
10 to 15 years	22

While many constitutional reactions and focal changes have been reported following the subcutaneous injections, we have never seen any serious results following the cutaneous use of tuberculin where even the simplest rules of cleanliness have been followed. We have seen only one case of systemic involvement which, we believe, could be traced to the intracutaneous use of tuberculin for diagnostic purposes. Thus we may say that the Pirquet test, especially in comparison with other tuberculin tests, is devoid of any danger.

SUMMARY

1. Tuberculin skin reaction is specific in its nature.

2. Except in the presence of certain well-defined pathologic conditions the tuberculin reactions are always positive in the

presence of tuberculous infection. In the absence of such exceptions a negative reaction, with proper technic, is of great value in differential diagnosis.

3. Tuberculin reactions are of great value in diagnosis in infancy and young children.

4. The intracutaneous tuberculin test is the most delicate and most reliable tuberculin test, the von Pirquet cutaneous test ranks next.

5. The tuberculin reactions should be considered in the light of adjuncts to careful clinical examination and observation, and not as definite means of diagnosis or establishing a prognosis.

6. They are also of great importance in the study of the etiology and prophylaxis of tuberculosis.

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CLINIC OF DR. FRANK WRIGHT

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NEPHRITIS

Determination of the Treatment of Each Case from the Findings.

The two patients about to be shown today give little difficulty in making a diagnosis of their disease—nephritis. They are presented because careful consideration of many of the findings is of distinct help in the treatment of people with diseased kidneys and has a decided bearing upon the prognosis in these cases.

If, at the outset, we take careful note of the fact that in all cases of nephritis there is diminished or delayed excretion of one or all of the urinary constituents, and that the close study of the rate at which these bodies are excreted, or the findings of a disturbance in the quantitative relation of these same bodies in the blood, rather than the determination of the amount of albumin or the number of casts, gives us the best information regarding the severity of the nephritis.

The manner in which urine is secreted under normal conditions has been the subject of discussion by physiologists for over seventy years; it is, then, not to be wondered at that the altered secretion in the various types of nephritis has been a puzzle that is of slow solution, and is as yet far from being satisfactorily explained. However, certain clinical facts recently brought to light do seem of distinct assistance in summing up the clinical picture, and these are the points I wish to emphasize today.

How the normal kidney is able to form from the blood-plasma a fluid of greater concentration and higher osmotic pressure than that of the blood has been a stumbling-block. The theory of "vital secretion" of Heidenhein fails to explain satisfactorily; the kidney does not "secrete" urine in the way that the pancreas secretes its juice or the submaxillary gland its saliva. Nor is

the kidney endowed with the power of picking out substances from the blood with uncanny accuracy, especially when these substances embody such a great variety as urea, alkaloids, dye stuffs, and salts.

The so-called "modern theory," well presented by A. R. Cushny in his monograph on the Secretion of the Urine, offers an accurate survey of the present knowledge of the subject. Quoting in part:

"The secretion of urine consists of two distinct processes, differing not only in site but also in nature. The first of these, the filtration, occurs in the glomerulus, and is purely physical; the second, reabsorption, occurs in the tubules and depends on the vital activity of the epithelium."

The energy supplied by the blood-pressure is not sufficient to perform the whole work of secretion, and the kidney itself furnishes the greater proportion of the energy required. The pressure in the glomerular capillaries suffices for filtration, and the capsule filters off the colloid substances of the blood, principally the protein, while allowing the rest of the constituents to pass through without alteration in their relative concentration; the glomerular filtrate is then practically deproteinized plasma. In its passage through the tubules this fluid is altered by the absorption of certain of its constituents by the epithelium; the passage of the absorbed water and solids of the glomerular filtrate is an active absorption.

Filtration, then, through the renal capsule is quite like that through any filtering medium dependent upon several factors: (1) the pressure on the proximal side of filter—if the capillary pressure be high more fluid is passed through—this has decided clinical evidence to support it; (2) the character of the membrane —the renal capsule shows variability in different individuals and in the same individual at various times. This is especially true in pathologic conditions; for example, when the oxygen supply is insufficient in cardiac decompensation, the resistance to permeation rises rapidly; (3) the nature of the fluid subjected to the process, the filtrand; because of the fact that the large molecules of the colloids (*e. g.*, the proteins) do not pass, an increase in the

quantities may lessen the rapidity of filtration by holding the water on the proximal side—conversely, a diminution in the amount of colloid following dilution by ingested fluid increases the amount of filtrate from the capsule.

Absorption, taking place in the tubules, is the means by which the glomerulus filtrate is changed in composition and concentration to the urine which passes out of the ureter. A great portion of the water is absorbed, as are the chlorids and practically all the dextrose. Sodium is absorbed readily, potassium with difficulty, which explains why potassium salts are useful as diuretics. The constituents of the plasma, called "threshold bodies," are taken up by the tubules in definite proportions, dependent upon their values in the blood; "no-threshold bodies," like urea, are not absorbed, but escape through the ureter. The cells lining the tubules absorb from the glomerular filtrate, then, a slightly alkaline fluid containing sugar, amino-acids, and similar food substances, chlorid, sodium and potassium, in about the same proportion in which they are present in normal plasma.

The function of the kidney may then be defined as the filtration of the non-colloid constituents of the plasma through the capsule, and the absorption of what is practically Locke's fluid through the tubules. The capsule provides the tubules with the fluid as it exists in the circulation, the tubules return to the blood the fluid best needed for the tissues, the rest escaping in the urine. If the plasma be too rich in chlorid or sugar, the filtrate retains the excess above the threshold amount, which is returned by the tubules. If the filtrate be dilute after heavy water ingestion the excess of water is left in the urine after the abstraction of the so-called optimal fluid by the tubules.

Turning now to the first patient we find a woman of twenty-five, a stenographer, first coming under my observation two years ago. Her mother died of pulmonary tuberculosis. At the age of fourteen she had a severe scarlatina, complicated by nephritis. At twenty-two and a half years repeated attacks of tonsillitis resulted in the removal of the tonsils. A few months later I saw her for the first time with a well-marked parenchymatous nephritis with secondary anemia of high grade—without doubt a re-

crudescence of a former nephritis. Rest, diet modification, and Basham's mixture resulted in improvement, and for nearly a year the patient has worked regularly; her urine showing little albumin and few casts.

January 6, 1918, she was seen with a fever of 103.6° F. due to a bronchopneumonia. At this time the urine was of the febrile type, 360 c.c. in twenty-four hours, 1030 gravity, containing much albumin, with many hyaline and granular casts. The recovery from the pneumonia was uneventful, the temperature being normal on the eighth day. The urine, however, became more scarce, and on the fourth day gave evidence of an exacerbation of the nephritic condition. This day 280 c.c. of urine, laden with a large quantity of albumin, blood-cells, granular as well as hyaline casts. Tympanites, pain in the lumbar region, a symptom popularly supposed to accompany a kidney lesion, yet rarely found unless the condition is quite acute, and vomiting followed. Edema began first in the lower part of the face, giving the appearance of a square, heavy set jaw, then pitting of the ankles and feet could be made out, and lastly, edema of the lids. The vomiting continued stubbornly. At this time examination of the blood for its CO_2, combining power, and of the alveolar air gave proof of a moderate acidosis. Administration of sodium bicarbonate promptly alleviated the vomiting, but was followed by very noticeable increase in the edema—the weight increasing 4 pounds the first day and more than 3 the second. On substituting chalk mixture complete cessation of all emesis resulted. Practically all salt was eliminated from the diet, yet the patient's weight increased from 114 to 138 pounds in twelve days. The diet was salt poor and non-nitrogenous, with restricted fluids until the vomiting ceased, when the Karrel plan was followed, with the result that the steadily increasing edema was brought to a standstill, then diminished slowly; the weight at present is 126 pounds.

In the meantime the loss of albumin in the urine has ranged from 4 to 11 grams daily, and the total loss in the fifty days of her illness has been approximately 345 grams. It has been estimated that the total amount of protein in the blood of an average individual is something over 200 grams, so that such a loss,

coupled with a restricted intake, might make a change in the serum protein in this particular individual. Estimation of the total protein, serum albumin, and serum globulin gave the following results:

	Total protein.	Serum albumin.	Serum globulin.	Globulin, per cent.
This patient.....	5.60 gm. per 100 c.c.	2.34	3.26	59
Normal persons.....	7.50 gm. per 100 c.c.	5.03	2.47	33

For comparison I have included the results obtained by analysis of the serum of a normal individual—figures which are quite in accord with those of other investigators, such as Epstein.

Normally in 100 c.c. of serum 6 to 8 grams of protein are found, of which approximately one-third is globulin, the remainder serum albumin. In this case in which the total protein is but 75 per cent. of what is usually found, the reduction of the amount of serum albumin is the striking feature. This is but half of the average quantity. The disproportion between the albumin and globulin is further emphasized by the high percentage of globulin, nearly 60 per cent., in place of the 33 found in the normal individual. The non-protein nitrogen was 36 mg., the urea 28, and uric acid 1.2 mg. per 100 c.c., all within normal limits. Coupled with this diminution of the serum albumin is the fact that the protein in the urine was practically all albumin, no globulin being found.

From these findings one may logically conclude—

(1) That the daily loss of albumin and not globulin in the urine, if continued a sufficient length of time, does influence the total protein content of the blood-plasma, especially the albumin portion of the protein.

(2) That in the management of such a condition steps should be taken to furnish protein to the circulation if satisfactory results are attained.

(3) Lastly, if the diminution of the protein content of the plasma be sufficient, the osmotic pressure may be so reduced that absorption or retention of fluid by the tissues is favored and edema easily results.

As applied to this patient the treatment instituted is first

for the modification of the edema—the use of the Karrel milk diet, using skimmed milk in place of whole, as most nephritics do not tolerate fats well.

Next, the transfusion of blood by the citrate method after the removal of an equal volume of the patient's blood. This has been done to good advantage by other clinicians; the abstracting of a sufficient volume to prevent overloading of the circulation, as well as to remove toxic material and lipoids, the infusion to increase the quantity of protein which we know to be deficient.

Lastly, and most important, the maintenance of a diet which will furnish protein, a moderate amount only of salt, and a quantity of fluid which is not excessive; about 1200 c.c. daily.

As for the foods used, I have found those suggested by Epstein to be of distinct aid. This list includes lean veal, lean ham, whites of eggs, oysters, gelatin, lima beans, lentils, split peas, green peas, mushrooms, rice, oatmeal, bananas, skimmed milk, weak coffee, weak tea, and cocoa. The amount of fat is kept at a minimum, and of carbohydrates about 200 grams, because of the tendency of water retention if too great quantities are ingested.

In the early stages I have also used amino-acids—*e. g.*, protein—a larger part of which is digested to the amino-acid stage.

This second patient is shown because the findings in his blood are so diametrically opposed to those of the first that the great range of symptoms and findings associated with disturbance of kidney function may be emphasized.

The man is a merchant, fifty-four years of age. Without going into detail about his medical history, I can say it was uneventful. He has had no severe illnesses, no venereal diseases. The man worked hard, ate too much and too hurriedly, smoked excessively, and drank moderately. Two years ago he applied for life insurance, was rejected because of abnormally high blood-pressure, after which, as he says, he became sick.

Physical examination at that time showed the findings so frequently noted; the moderate enlargement of the heart to the left, the accentuated second sound in the aortic area, a systolic blood-pressure of 190, diastolic 112. The urine was of low specific gravity, 1012, large in amount—2100 c.c.—gave a faint test for

albumin, and microscopically a few granular and hyaline casts were seen.

The Mosenthal test for kidney function gave evidence of a tardy excretion of fluid and nitrogen and an inability to concentrate, the specific gravities varying but little during the twenty-four hours. The amount passed at night was large. The phenol-sulphonephthalein excretion was low—38 per cent. in two hours.

During the two years that have elapsed the patient has followed directions explicitly and changed his whole mode of living. He works but four hours a day, taking frequent vacations; he does not smoke or drink, and his diet has consisted exclusively of milk, buttermilk, cooked and green vegetables, nuts, cereals, stewed and raw fruits. He has lost 15 pounds, his weight at present being 154. His systolic blood-pressure today is 162, diastolic 104.

The point I wish to emphasize is the clinical findings in the blood:

Milligrams per 100 c.c. of Blood

	Non-protein nitrogen.	Blood urea.	Uric acid.
Today	44	39	3.3
22 months ago	62	48	Not estimated.

For comparison I add the findings in the blood of the first patient.

Milligrams per 100 c.c. of Blood

Non-protein nitrogen.	Blood urea.	Uric acid.
36	28	1.2

The estimation of the serum proteins was made in this case also. For contrast I will append the findings of the first patient and then of the average:

Grams per 100 c.c. of Serum

Second patient.	Total protein.	Serum albumin.	Serum globulin.	Globulin, per cent.
Chronic interstitial nephritis and hypertension	8.2	5.7	2.5	30
First patient.				
Chronic parenchymatous nephritis	5.6	2.3	3.2	59
Average normal individual	7.50	5.03	2.47	33

To sum up the findings in the two cases:

Both show a disturbance of excretion by the kidney and a changed relation of the constituents of the blood.

The first case, that of chronic parenchymatous nephritis, attracted attention by the diminished excretion of water and large quantities of albumin in the urine, while from the standpoint of the blood a poverty of serum albumin with resulting edema. There is no retention of non-protein nitrogenous constituents.

The second case shows a large excretion of fluid by the kidney, very little albumin, a lagging as to rate of excretion, too large a portion being left for excretion at night, and a fixation of specific gravity at a low figure.

In contrast to the first patient the disturbance in the blood relationship is evidenced by a retention of the non-protein nitrogenous bodies, while the protein content is undisturbed.

The bearing of these facts as to management is quite clear. The patient with parenchymatous nephritis requires, first, active steps to combat the edema; second, to replenish the lost albumin. This means the feeding of protein containing foods which are readily assimilated—at the same time restricting the quantities of fluid, fat, salt, and, to a less extent, carbohydrate. To bridge over the stage following the diminution of the edema transfusion of blood and the feeding of protein disintegrated to the amino-acid stage is to be recommended.

The patient with interstitial nephritis and hypertension is the one requiring careful and constant supervision and restriction as to diet. This particular individual even with care extending over a period of two years still has abundant evidence of the retention in his blood, and while the kidney may excrete enough for his immediate needs, he can ill afford to burden his excretory organs with even a slight excess of protein.

The fact that the human body often does better with a few smaller amounts of protein than is usually eaten will be brought home to many of us through the food restriction imposed by the great war—and undoubtedly to our benefit.

CLINIC OF DR. ARTHUR F. BYFIELD,

COOK COUNTY HOSPITAL

SPLENOMEGALY AND CIRRHOSIS OF THE LIVER

January, 1918.

LAST month there came to my service almost simultaneously two young men who passed through the receiving ward with the same diagnosis, namely, Banti's disease. The study of these two cases, which has just been completed, furnishes data which emphasize, in an especially illuminating way, it seems to me, the very close relationship of the Banti picture to the Laennec type of cirrhosis of the liver.

If our time permits, I plan to carry you beyond the consideration merely of this relationship and to take up briefly the problem of the cirrhoses as a whole, from the point of view of the splenic and hepatic changes in the same. Your texts concern themselves chiefly with more or less pure types of Banti's disease, Laennec's cirrhosis, Hanot's cirrhosis, etc., and pay too little attention to the not infrequently encountered mixed or transitional forms. It is these mixed forms, which one finds difficulty in classifying clinically and often anatomically, that are most instructive, and which, in my opinion, indicate that the Banti complex and the different cirrhoses are properly to be regarded not as entities, but as parts of one large process modified in the individual case by the nature, action, and localization of the responsible toxin.

As both of the patients have left my service I shall make use of the hospital records to give you the necessary data.

CASE I.—(F. P., Patient No. 652,544, Ward 63).

The first patient is an Italian, twenty-four years old, who has been in America for seven years and has lately been employed in the steel mills.

His present complaints are practically all of seven months' duration. They are: 1. Dull pain, or a feeling of weight, in the upper left abdomen, first noticed when he stooped or bent over, but present now also when he takes a deep breath. 2. A swelling in the same region. 3. Loss in weight, amounting to 25 pounds. 4. Weakness. 5. Diarrhea, with bloody stools, the latter not being verified by our laboratory. 6. Epistaxis at irregular intervals. Hematemesis is denied.

Fig. 245.—The outline of the spleen in Case I. Weight, 1310 grams. Measurements, 25 x 15 x 10 cm. (maximum thickness).

The only previous illness was during a period of four or five months, five years ago, when he had paroxyms of chills and fever. The venereal and family data are negative, and as to his personal routine there is little to note except that he smokes and drinks beer moderately. The use of whisky or gin is denied.

The physical examination shows a man of fair nourishment, considering his long illness. The scleræ convey a suggestion of icterus, though the color of the skin is hardly more than racial.

The temperature, pulse, and respiratory rates have been normal at all times since he entered the hospital.

Until the abdomen is reached the examination is entirely negative except for the presence of a few small, discrete, nontender lymph-nodes in the cervical chains. The blood-pressure readings are $\frac{152}{100}$ mm. Hg.

The spleen is enormously enlarged, causing a marked prominence in the left upper quadrant of the abdomen and the lower axilla (Fig. 245). The organ is firm and the surface smooth except for a small knob-like prominence just below the costal arch.

There is no palpable notch. Over the upper lateral aspects of the abdominal portion of the tumor a loud, rough, to-and-fro friction-rub is heard.

The liver does not appear enlarged either by palpation or percussion, and there is no free fluid in the abdomen. The balance of the physical examination is negative.

Laboratory Data.—The urine is normal in every particular. The stool is mushy, of normal color, and contains no chemical blood. The Wassermann reaction in the blood is negative. A provocative dose of neodiarsenol (0.6 gm.), followed in five days and again in ten days by Wassermann tests, produced no change in the reaction.

The hematologic examination revealed the following:

Hemoglobin, 68 per cent. (Sahli corrected).

Red blood-corpuscles: 3,930,000, the cells showing a moderate anisocytosis, with a small-celled tendency, moderate poikilocytosis, and rather pale centers.

White blood-corpuscles: 2400 (and 2600), distributed as follows:

Polynuclear neutrophils, 82 per cent.

Lymphocytes, 11 per cent.

Large mononuclear and transitional cells, 5 per cent.

Eosinophils, 2 per cent.

No malarial parasites were found.

Observation of the patient brought out one additional fact, namely, on two attempts to remove the stomach contents after a test-breakfast, there being an interval of three days between the attempts, a considerable amount of bright red blood came through the tube on each occasion. The introduction of the tube was without difficulty and could scarcely be held responsible for so large a hemorrhage. In other words, this manifestation—hematemesis—may properly be interpreted as a latent symptom.

An elaborate differential diagnosis in this case is quite unnecessary. Clinically, the picture is that of splenic anemia, which is a synonym for the initial stage of the disease first fully described by Banti and bearing his name. The occurrence, particularly in a young or middle-aged man, without discoverable

etiology, of a marked splenomegaly, associated with an anemia of the secondary type plus leukopenia and a relative lymphocytosis, and with hemorrhages from the mucous membranes, especially hematemesis—the whole exhibiting an exquisitely chronic course of three to five years or longer—is clinical justification, according to the criteria laid down by Banti, for the diagnosis of the first stage of the disease in question. With respect only to the relative lymphocytosis does our case deviate from these criteria, and there appears to be a considerable difference of opinion as to the validity of this point.

The matter of the present-day interpretation of Banti's disease I shall postpone for the moment.

In the case of the young man we are considering it appeared that the spleen was somewhat reduced in size after the first injection of neodiarsenol. For that reason, antiluetic therapy (diarsenol and mercury) was continued despite the negative Wassermann reactions. No further change was noted, however, after a month of this régime.

At another time we have discussed the indications for splenectomy in various conditions in which it has been advocated. In one process—the congenital form of hemolytic icterus—its success is admitted by all. In others, such as pernicious anemia, in which for a time the operation seemed tc hold out considerable hope, splenectomy has been more or less generally condemned. In Banti's disease opinion is still divided. While the splenomegaly in the latter is not merely a symptom as it is in pernicious anemia, it is also not so definitely the site of the essential pathology as in hemolytic icterus. The spleen of the Banti's process appears to be the point at which the pathogenic agent exerts its initial and most distinctive action. The course of the disease offers convincing proof, it would seem, that the second stage of the process does not begin until the splenic changes have reached a definite level. In selected cases, therefore, there may be said to exist the *relative* indication for splenectomy in Banti's disease. As the case we have been considering seemed to fall into that category—an early one in an individual in fairly good physical condition—operation was advised.

Operation and Pathologist's Report.—The removal of the spleen was not attended with especial difficulty, although there was considerable bleeding following the separation of the abundant adhesions about the organ. The liver was found normal, the peritoneum was smooth and glistening, and there was no free fluid in the abdominal cavity.

The patient has made a good recovery, and at present—about a month after the operation—feels very comfortable. Of course, an ultimate conclusion as to the success of the procedure cannot be drawn for years. The most striking change noted in our patient has concerned the blood-picture, the leukocytes now numbering about 10,000 per c.mm., and the red blood-corpuscles having passed the 4,000,000 mark.

Our pathologist, Dr. Nuzum, has made the following report: The spleen is enormously enlarged, weighing 1310 grams, and measuring 25 cm. in length, 15 cm. in breadth, and 10 cm. in thickness at the thickest point. It presents a uniformly dark purplish-red color. The capsule is tense and smooth except for an area over the diaphragmatic surface and extending backward over the posterior border, where there is an elevated, grayish-white fibrous thickening which measures 12.5 by 7 cm.

The gastric impression is very marked. There is no notch on the anterior border of the spleen. The splenic artery and vein exhibit no thrombosis.

Microscopically, the capsule appears thickened and the trabeculæ prominent. There is a moderate degree of fibrosis of the splenic pulp. The malpighian bodies have largely disappeared, while those which remain are sclerosed or almost completely replaced by connective tissue. The venous sinuses throughout the parenchyma are hyperplastic and dilated.

Paraffin sections of the spleen were stained by Levaditi's method and with carbol fuchsin. No spirochetes or tubercle bacilli were found.

Blood from the spleen examined after the removal of the organ showed no malarial parasites.

Résumé.—We have said that the clinical diagnosis in this case could not be other than the splenic anemia stage of Banti's

disease. This diagnosis is confirmed by the anatomic examination, which shows the prevailing change to be one of fibrosis. The rather moderate degree of the latter indicates that the process is fairly early and is harmonious with the clinical history. The absence of a discoverable etiology in this case stamps it as a true Banti's disease if one is inclined to adhere to the criteria laid down by Banti himself.

CASE II.—(J. S., Patient No. 654,733, Ward 63).

As I read you the record of this second case you will note how closely, in many respects, it resembles the first; you will note, also, certain important points of difference.

This is also the case of a young man, twenty-one years old, native born, and a janitor by occupation.

His complaints are of weakness, loss of weight, dyspnea, bloody stools, diarrhea, and abdominal pain. The weakness has been progressive for the past two years, while during the same period he has lost 25 pounds in weight. Shortness of breath has been noticed for a year. The diarrhea began a little over a month ago and has lately been succeeded by severe obstipation. At first the stools were black, but of late they have contained fresh blood.

The pain is colicky and intermittent and began about the time when blood appeared in the stools. It is often severe enough to prevent sleep, and is usually relieved by a bowel movement, and, to some extent, also, by local applications of heat. Though the pain has been of maximum intensity in the left upper quadrant of the abdomen, it has been severe at times along the entire course of the colon.

There is a history, also, of an hemoptysis, amounting to ¼ tumblerful, four months ago, but we have not satisfied ourselves that the blood was not of esophageal or gastric origin. Since the patient entered the hospital he has had a number of severe attacks of epistaxis.

The anamnesis contains only one additional fact of importance, namely, that the patient is an immoderate user of alcoholic beverages.

The findings are, for the most part, normal. The patient is

slender, though fairly well nourished. There is no jaundice and no other abnormal pigmentation. No pathology is evident in the superficial groups of lymph-nodes and there is no ankle edema. The head and neck and the heart and lungs reveal no changes of significance. The blood-pressure readings are $\frac{136}{86}$ mm. Hg.

The abdomen is slightly distended and exhibits a considerable prominence in the left upper quadrant. A moderate degree of

Fig. 246.—The splenomegaly in Case II. Weight, 810 grams. Dimensions, 20 x 12.5 x 9 cm. (greatest thickness).

tenderness, without rigidity, is present along the course of the large bowel, and particularly in the splenic region, where a large, smooth, rounded tumor, which moves freely with respiration, can be palpated. The size of this tumor, which presents all of the diagnostic criteria of the spleen, is shown in the photograph I have here (Fig. 246).

In this case, unlike the first, the liver seems to be somewhat enlarged, extending upward to the fifth rib and downward two

fingerbreadths below the costal arch. The consistency is somewhat firmer than the normal, there are no gross inequalities of the surface, and the edge is moderately round. There is no free fluid in the peritoneal cavity.

Inasmuch as digital examination of the rectum failed to clear up the cause of the bloody stools—the few, small, dilated hemorrhoidal veins did not seem to offer a sufficient explanation—the sigmoidoscope was passed. No pathology of significance was revealed.

The laboratory has made the following reports:

Urine: Negative in all particulars.

Stools: Normal except for the presence of chemical blood.

Wassermann reaction: In the blood, negative.

Hematologic examination:

Hemoglobin, 45 per cent.

Erythrocytes, 2,400,000, and on a second enumeration, 2,200,000. The cells showed the characteristics of a moderate secondary anemia.

Leukocytes, 2600, and on subsequent counts, 3000, 2000, 2400, 2800, distributed as follows:

Polynuclear neutrophils, 62 per cent.

Lymphocytes, 35 per cent.

Large mononuclear and transitional cells, 3 per cent.

If, for the moment, we leave out of consideration the history of alcoholism, we are fully justified, on the basis of the various data just given you, in making a diagnosis of Banti's disease in this second case, for reasons already given in the discussion of Case I. In one important respect, that of the enlargement of the liver, the second case differs from the first. On the strength of this hepatic change, still assuming that we have to do with Banti's disease, we must conclude that Case II is in the second stage of that process.

Returning now to the matter of the alcoholic history, we are forced to dismiss the possibility of Banti's disease in this young man if we adhere to the strict clinical standards laid down by Banti himself, one of the most important of which is that there must be no discoverable etiology. It is possible, of course, that

an alcoholic should develop the Banti picture and that the alcohol is incidental, not responsible. This, however, is merely begging the question.

Allow me to call your attention at this point to what may be termed the present-day conception of Banti's disease. It is pretty generally conceded that the strict clinical and pathologic criteria essential to a diagnosis laid down by Banti in his several communications can no longer be accepted in their entirety. I have already stated that splenic anemia, formerly regarded as an entity, must be incorporated into our conception of the Banti picture, of which it is the initial stage. Of more importance, perhaps, is the present tendency to regard Banti's picture not as an entity, but as a symptom-complex which may be due not only to causes not evident, but to the toxins of such conditions as syphilis, malaria, tuberculosis, and to alcohol.

This revision of the Banti formula is based upon excellent clinical and pathologic grounds. Anatomically verified cases of Banti's disease show clearly that the clinical picture is subject to considerable variation. Conversely, cases clinically fulfilling the Banti postulates prove ultimately to be due to syphilis, alcohol, malaria, etc. Nor, finally, is the pathology of cases which clinically bore every mark of the true Banti picture, including the absence of a cause, always uniform.

In brief, there exists every reason for believing that Banti's disease is not an entity, but a complex of variable origin and variable clinical picture. Hence, as suggested on several sides, it seems advisable to discontinue the use of the term "Banti's disease" and to substitute therefor a more correct application, such as the "Banti symptom-complex" or the "Banti complex."

On the basis of the history and findings of the patient under consideration and in view of what has just been said regarding the meaning of Banti's disease, I feel fully justified in making a diagnosis of the Banti complex in this second case.

From an academic point of view, however, it is interesting in this case to analyze the factors which, on the one hand, speak for the pure Banti picture and, on the other, for the diagnosis of the ordinary Laennec cirrhosis of the liver. As a matter of fact,

the clinical findings point partly in one direction, partly in the other. It is a *mixed case* and, therefore, especially instructive. The age of the patient, the marked splenomegaly, the typical blood-picture, and the hemorrhagic diathesis speak for Banti's disease in the strict sense. The history of alcoholism and the relatively short duration of the process—two years or less—speak for cirrhosis. But as we have already noted with respect to Banti's disease, and as we shall have occasion to point out later in connection with cirrhosis, the clinical pictures of both are subject to such considerable variation as to offer no safe basis for a differential diagnosis. Clinically, all that can be said, as we have already indicated, is that we have to do with a case of the Banti complex, due, perhaps, to alcohol.

This patient was also transferred to the surgical service. My recommendation was that an exploratory laparotomy be done to ascertain, if possible, the cause of the man's more or less generalized abdominal pain and his recently developed intractable constipation, manifestations which did not harmonize with either of the diagnoses mentioned above. Incidentally, it may be said, the possibility of a tuberculous peritonitis was not entirely disregarded, either as a complication of an alcoholic cirrhosis of the liver or as a process secondary to that rare form of primary tuberculosis of the spleen, described by Carbone and Auché, in which the clinical and anatomic pictures are essentially those of the Banti complex.

At operation the peritoneum was found normal and the peritoneal cavity free from fluid. Associated with the considerable splenomegaly was a moderate degree of perisplenitis. The liver was moderately enlarged and exhibited a typical hobnail surface.

Exploration, in brief, revealed no cause for the severe pain or the obstipation, and in particular eliminated tuberculous peritonitis as a possible cause for the same. As regards the pathology of chief interest to us, operation left undecided whether the case was one of Banti's disease in its second phase (using this term in its strict sense), or a Laennec cirrhosis of the liver with an unusually large spleen.

Instead of closing the abdomen at this point, the advisability

of splenectomy was considered. The question was argued from the standpoint of the diagnostic possibilities, and it was decided that whether the case was one of Banti's disease in the stage of hepatic cirrhosis without apparent etiology, or an alcoholic cirrhosis with an unusually marked splenic enlargement, the indication was present to remove the spleen upon the following grounds:

1. The age of the patient; 2, the various manifestations pointing more to the strict Banti type than to a Laennec cirrhosis; 3, the relatively short duration of the process; 4, the probability that the spleen was in some degree at least a focus of further infection; 5, the organ in its present state was of as little value in the economy as a diseased tonsil or appendix.

Kanavel[1] has well expressed the indications for splenectomy in this type of case. He has recently said: "In splenic anemia and Banti's disease, especially in their early stages, the results of splenectomy are . . . extremely encouraging. . . . In these cases (splenic anemia, Banti's disease, and the anemias secondary to syphilis, chronic sepsis, and malaria) we have to do, apparently, with an anemia resulting from a hypertrophy of the spleen, the enlargement being the consequence of a toxemia. The splenic hypertrophy is probably beneficial in limiting or destroying the primary condition, but carries with it the detrimental consequence of an abnormal destruction of the red blood-corpuscles. If the splenomegaly represents merely the aftermath of an infection which has already run its course, the removal of the organ will be sufficient to relieve the anemia.

"We can speak with less certainty of those splenic enlargements accompanying the various cirrhoses of the liver. In those cases in which it can be shown that the causative agent has *primarily* involved the spleen, benefit can be expected from operation, while in conditions in which the splenic hypertrophy is distinctly secondary to the hepatic process, little good can be expected."

The spleen was accordingly removed. The operation was attended with little hemorrhage and shock. Unfortunately,

[1] Medical Clinics of Chicago, II, 2, September, 1916, p. 414.

however, the early favorable postoperative course was interrupted on the third day by a bronchopneumonia to which the patient rapidly succumbed.

The pathologic laboratory has made the following report on the spleen from this case: Weight 810 grams; dimensions 20 by 12.5 by 9 cm. (maximum thickness). The color is the normal purplish-red hue. The capsule is tense and the splenic pulp soft and engorged with dark blood. The vessels at the hilus of the organ are not thrombosed.

Microscopically, the capsule appears of normal thickness. There is a slight increase of connective tissue—a fibrosis of the splenic pulp. The malpighian bodies appear entirely normal. The venous sinuses are hyperplastic and dilated and the cells of the parenchyma have partially disappeared, giving the appearance of empty spaces between the dilated sinuses.

No Spirochætæ pallidæ nor tubercle bacilli could be found by suitable staining methods.

A section of the liver removed after death (a complete autopsy was not permitted) shows the features characteristic of an atrophic cirrhosis.

In the light of generally accepted criteria the anatomic findings in this case offer a no more satisfactory solution of the exact nature of the process than do the clinical. We may still speak of it as a "mixed" case. The moderate degree of fibrosis is common both to the Laennec type of cirrhosis and to early cases of Banti's disease. The evidence of stasis suggests the spleen of cirrhosis; the absence of the characteristic hyperplasia of the pulp speaks against cirrhosis. The size of the spleen, while unusual for the alcoholic cirrhosis, is by no means impossible in the same.

I believe that the data furnished by these two cases into which we have entered in so great detail show very conclusively the close relationship existing between Banti's disease, *sensu strictu*, and the Laennec type of hepatic cirrhosis. This is the impression I wish you to carry away from the discussion of these records. A great many observers go a step further and maintain that the two conditions are essentially one process, the toxic agent in one

affecting primarily and predominantly the spleen, and in the other the liver and spleen simultaneously and more or less equally.

This conception leads us directly to what I have called the incidental part of my theme—the problem of the cirrhoses as a whole from the point of view of the splenic and hepatic changes in the same. The following considerations will assist us in arriving at a solution of this problem:

1. On the basis of the material already given you we may, without undue assumption, classify splenic anemia and Banti's disease under the cirrhoses of the liver. In our further discussion, therefore, the two conditions will, with certain exceptions, be considered together.

2. Just as Banti's disease—strictly interpreted—and Laennec's cirrhosis merge into one another, so do the Laennec and the Hanot types of cirrhosis exhibit mixed or transitional forms. These mixed types, which are not at all infrequent, though given scant attention in your texts, resemble the Laennec cirrhosis in their alcoholic history and age incidence, and the Hanot cirrhosis, particularly in the matter of a very large spleen and the occurrence of icterus. Clinically, the liver is variable; anatomically, it exhibits characteristics of both the alcoholic and biliary cirrhosis.

3. Just as there are cases which may be regarded as representing transitions between Banti's disease and the Laennec type of cirrhosis, and further between the hobnail and the Hanot types, so may cases of the latter approach closely the clinical and anatomic pictures of Banti's disease. The age of the patients, an unusually large spleen, icterus, hemorrhages, and a degree of fibrosis not usually found in the cirrhotic spleen are the findings which bridge the two processes.

4. As to the spleen in the various conditions under consideration, it may be said that although a moderately enlarged organ is the usual thing in alcoholic cirrhosis, an enormous spleen in Banti's disease and a spleen of intermediate size in Hanot's cirrhosis, yet the variations from this rule observed in anatomically verified cases are considerable. Thus, in this particular also,

there exists no absolute criterion by which the conditions may be distinguished.

As regards the spleen, further, the emphasis formerly placed upon the rôle of stasis in causing the splenomegalies of the cirrhosis has gradually given way to the opinion now almost universally held that the enlargement is due equally, if not predominantly, to the action of the hypothetic toxin held responsible for the cirrhotic process as a whole. This conception establishes another point of contact between the spleen of the cirrhosis and that of Banti's disease.

5. With respect to the matter of jaundice, no significant data can be offered. In the Laennec cirrhosis and in Banti's disease the degree of icterus is usually slight, while in Hanot's cirrhosis the subicteric level is disturbed periodically by summits of intense, though not acholic, jaundice. As a variation of this rule, however, we have been impressed by the frequency of jaundice, of no mean degree, in the Laennec type, due, probably, to the same factors which are responsible in the hypertrophic form, namely, a cholangitis and possibly changes in the liver parenchyma itself.

6. Too great emphasis has been laid perhaps upon the blood-picture in the splenic anemia phase of Banti's disease. It is not at all an uncommon thing to find a marked leukopenia and an anemia of the secondary type in undoubted cases of hepatic cirrhosis. There is a case of the latter in my service at present with 3000 white blood-corpuscles to the cubic millimeter, an erythrocyte count of 3,500,000, and a hemoglobin of 60.

7. Hemorrhages from the gastro-intestinal tract are common to all of the conditions we are considering.

These are some of the more important facts which render so difficult a classification of the cirrhoses on clinical or anatomic grounds. Indeed, observers are in accord in pointing out that no satisfactory classification is to be hoped for until one can be constructed on an etiologic basis.

To me the problem seems less difficult of understanding if regarded in some such light as this: The cirrhoses of the liver, splenic anemia, and Banti's disease, together with the many mixed forms we have considered, are all manifestations of one

large process. The type assumed in the individual case depends upon factors imperfectly understood, but which, from analogy with pathologic processes more fully analyzed, may be assumed to be the nature and mode of action of the responsible agent and the resistance of the individual as an entity and as regards certain of his organs (spleen, liver, etc.).

This responsible agent is generally supposed to be of the nature of a toxin, in many cases unknown—possibly a metabolic by-product—in others known (syphilis, malaria, tuberculosis, alcohol—the latter directly, or indirectly, by creating conditions favorable to the production of metabolic poisons). In one case the initial and predominant action of the etiologic agent is exerted on the spleen; in another, more or less equally and simultaneously, on the liver and spleen; and in still others primarily on the liver. The transitional types spoken of would be interpreted along similar lines.

This conception, while based partly upon theory, has much of fact in its favor, and seems to offer the best explanation, at present available, of this difficult problem.

CLINIC OF DR. RALPH C. HAMILL

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INSOMNIA

LYING awake at night seems to possess more terrors for the adult human than almost any other departure from the normal. Failure of sleep, or insomnia, doubtless has many different causes or, to put it better, many things contribute to the restlessness, nervousness, worry, etc., that keep people awake. I want to tell you of a case whom, unfortunately, I cannot demonstrate, but, after all, demonstration of such cases is not of great importance.

The case is that of a physician who is about forty, and who has had a hard battle to fight all his life. There are many elements in this battle that I do not feel entirely free to mention, or at least to dwell upon. One of the elements which make the battle hard is not one that a person would ordinarily be inclined to take into consideration. It is the fact that he graduated from an inferior medical school. That is, he did not have adequate preparation upon which to base his life-work. Also, he was married to a young woman who was mentally deficient and who has made a great deal of trouble for him. This trouble is an interesting part of the problem to evaluate.

To digress a little, I must ask you to appreciate the fact that, after all, we humans are essentially egoistic, that is, essentially selfish, so that any interference with our progress necessarily causes trouble in our minds, bringing up a conflict between the natural selfishness which demands our doing our best for ourselves, and the more cultured attitude which demands self-sacrifice and our doing our utmost for the sick and inefficient.

This man, then, had that problem to wrestle with, namely, a realization that the person he was married to was a liability

rather than an asset. That he lost instead of gained every day that he had to live with her. After wrestling with his problems for a few years he began to sleep poorly, and in order to do his work the next day he felt it was absolutely essential that he get a good night's sleep. In order to get this sleep he commenced to take drugs. He used veronal, trional, sulfonal, bromids, and all the rest of the sedatives except opium, until he ceased to be able to get any satisfaction from them. Then he turned to alcohol. At first he used a small amount of beer, but gradually increased the amount, and then found that it knocked his stomach out, and so turned to whisky. For the last few years he had been using a constantly increasing amount of whisky in order to secure unbroken slumber. This amount had finally gotten so large that he felt the effects the next day in a slowing down of his mental capacity, and he realized that the time had come when he had to break with whisky. Consequently, he consulted me with this tale to tell.

What was to be done for this doctor? What were his problems? First and foremost was a belief that in order to do his work creditably he had to have sleep; stated differently, his work and the excellence of its performance is the all-important factor, and this gives us a suggestion of that which I have already spoken of, namely, the natural, egoistic, selfish foundation of our behavior. His work, his success is the important thing. That is the first element of his problem. It seems to me that the first element of my problem is to straighten this one out. To do this I have to determine as best I can what sleep really is and what it does, and also, what is more important, the patient must see his needs and understand them. He must understand why he thinks sleep is so essential.

I think we can readily appreciate, at least those of us who are old enough, that so far as the physical side is concerned—the physical fatigue—sleep is not nearly so essential to the ordinary adult of thirty or more years as it is to the younger person. That is, we do not take sufficient physical exercise, we do not exercise so much, but that we can get a rest by simply lying still sufficient to put us on our feet the next day. We do not expend anywhere

near as much physical energy as we do when we are younger. Consequently, I cannot believe that unconsciousness with its still-lying or absolute quiet is an essential. On the contrary, we adults have much need for mental relaxation, or at least our daily problems are more difficult than those of the adolescent. The moderately successful adult has to coerce and drive his mind along a single-track road practically all day long if that moderate degree of success is to be continued. The more successful he is, the more single tracked the road. It is not so difficult to keep one's mind on the track if the attendant circumstances are in favor of doing so. The attendant circumstances are the character of the mind—that is to say, its fitness for the task, the degree of interest with which the mind takes up its work, which, to be sure, is somewhat dependent upon the fitness, and somewhat dependent upon this interest, the number of distractions that attempt to side-track, switch, or wreck this single-tracked progress. We are all agreed that "all work and no play makes Jack a dull boy." We have always said that vacations are absolutely necessary. Consequently, I am inclined to think that sleep is very little more than a daily vacation from these driving powers of our concentration or attention, will power, memory, or what you will. Sleep is really a departure into vacation fields of the tired out mentality. It is tired out, as I have pointed out, in proportion to the difficulty of its tasks, and this difficulty is dependent not upon the tasks alone, but upon many additional attributes.

In this case the inferior alma mater, the inferior preparation, was sure to make for difficulty. This man is an unusually conscientious, ambitious man. He was tremendously driven by the necessity of doing well by his patients, consequently it was much harder for him to practice medicine than it would have been if either his education had been better or his conscience tougher. All this I laid before the doctor.

It seems to be an inevitable impulse of the human mind to look for cause, and when we suffer it is almost inevitable that we should think that the suffering comes as a form of punishment of some variety. We see this expressed in all sorts of ways

—"Why should I have to suffer this way?" "Mary always went to church; she was the best woman in the world, why did this overtake her?" etc.—we hear it on all sides every day. How does this apply to our patient? He suffers, he lies awake, he is more or less unhappy. He has a problem on his hands that almost demands independent, egoistic action, and yet, on the other hand, demands much of self-sacrifice. A man has so much energy to expend and no more, so much time to devote and no more. For the reasons cited above, time and energy were demanded by both his practice and his wife in such a degree that drive himself though he would still he could not do enough to satisfy himself. He had to try to strike a balance somewhere between these two extremes of egoistic action and self-sacrifice. It would be surprising indeed if self-sacrifice ruled entirely. Consequently, here alone we see possible cause of self-condemnation —he does not give up as much as he might for the benefit of the mentally deficient wife. Perhaps the most frequent thought of blame that occurs to those who suffer functionally in a nervous way is the thought of how disastrous the effects of masturbation may have been. The thought that masturbation will be followed in later years by insanity, "loss of manhood," nervousness, etc., has been well sown in fertile ground by quacks, patent medicine houses, and oversolicitous elders. And so, as this man's difficulties increased and his mind became more and more unsettled as to what should be done, he commenced to doubt himself, to lose his self-confidence. His memory wasn't so good—of course no one's is who is worried and harassed. He became irritable, which was not creditable. There undoubtedly were moments, if not longer periods, when he began to wonder if insanity might not be his fate. You will remember that he was living with it and in apprehension of what it might do to him through his wife.

This fear of insanity, loss of mental control, is perhaps the most insidious as well as the most wide-spread of the fears of our fellow-men. They do not like to own up to it, so the physician frequently must ask directly whether it is present or not. Then he must do his utmost to explain its genesis. If he can do

this, in the majority of cases the patient's relief is at once apparent.

This man's wife belonged to a very religious family, a fact that is not without importance. The belief in sin was active enough in his environment, at least, if not in his own mental make-up. All this side of the problem, namely, the side of sin and punishment, had to be laid before him so that he could see in the open things that he might allow himself to barely glimpse or suspect after dark.

About two years ago a man fifty-five years old consulted me with very much the same story, except that the element of the mentally enfeebled wife was not present. Business difficulties, the fear of failure, of business inefficiency, and an insomnia that had lasted for twelve years were the principles of his complaint. For the past twelve years he had been depending upon whisky for his rest. He was thoroughly convinced that he had to have sleep in order to be able to work the next day, and he felt certain that he could not sleep without whisky. He had started in moderately, as had the first man, but had gradually increased the amount until at the time he consulted me he was drinking over a quart a day. Of course he was feeling it physically. He had gradually gotten to a point where he had to have a drink in the morning to brace him up, another drink at noon to carry him along, and in the middle of the afternoon he commenced to prepare for slumber. One might have said that he was obsessed with the idea that he would not sleep, or one might have gone still further and said that he wanted to be obsessed by this in order to have a good excuse to drink. There is more about this point than appears at first sight. Whisky, as you probably know, gives a person a certain feeling of efficiency; it lessens our self-condemnation and self-criticism and increases our egotism. It has a certain power to diminish our feelings of inadequacy. In this sense it is a natural substitute for a condition of sleep, because in our sleep we shut out all the distracting, overwhelming, overbearing, superior forces of the outside world. With these shut out we are master of all we survey. So, as I say, whisky

and sleep are natural partners. This man was taking sufficient whisky during the day so that there was very little danger of signs of his inadequacy overtaking him.

To this man I told the foregoing beliefs concerning sleep. Also, my belief that he would be able to work in spite of the fact that he had no sleep. I then told him to cut out the whisky entirely, go out after supper and take a good brisk walk for half an hour, then go home and take a warm bath for fifteen minutes, go to bed and lie there, and think of all the good times he had ever had, and when the pressure got too great merely turn over on his face and let nature take care of the rest. I also gave him some 15-grain sodium bromid tablets. He did not know what they were. He was to take one after breakfast and lunch and two after supper and at bedtime. The next day he called me up to tell me that the scheme worked perfectly. This after twelve years of whisky as the only possible means of sleep.

I will not attempt to determine the exact value of correcting the attitude of the patient toward the whole matter of sleep as against the value of the drug—the sodium bromid. In the case of the doctor no drug was used, and yet the simple procedures succeeded. With the older man, the second patient, sodium bromid may have had some effect. He had had 60 grains when he went to bed the first night. I would rather say that the two procedures, the talk and the drug, aided each other in their actions. Sodium bromid in good-sized doses certainly has a quieting effect. The patient has been reasoned with and made, or at least the attempt has been made, to have him take a reasonable attitude toward his problems. He is assured that he will sleep all right if he takes such a reasonable attitude. He goes to bed slightly fatigued physically from his walk after supper, which he thinks he knows is a healthy thing to do. His fears are somewhat quieted by the reassurances of the physician. He sleeps, and he certainly is not sure that the changed attitude is not the cause of his sleeping. If it is, then, in a sense, it is his own doing. That makes for increased self-confidence, and that is really what we want for the patient.

To return to my doctor. I gave him much the same directions, and because it was very cold weather when I saw him I directed him to crawl in between blankets instead of cold sheets. He reported to me the next day that a most astonishing thing had occurred. He had gone to bed at 9 o'clock, had immediately gone to sleep, and the next thing he knew it was 11 o'clock the next morning.

As I have said, he was given no drug and yet he slept as he hadn't slept for a long, long time. Consequently we can say without reserve that it was the changed attitude with him that brought the sleep. Suppose we say for a moment that it is his confidence in me that worked the cure. I will admit that in any therapeutic procedure a generous discount must be allowed for just this thing: The patient's faith in the physician. Now if the physician sticks to truth with his patient, then isn't it reasonable to expect that the patient, sensing the truth, will come to take a more reasonable and less emotional attitude toward his difficulties? If the truth is told, *i. e.*, in a general way, it is apprehension that keeps the patient awake and the fears are groundless; if that is fully grasped by the patient then he can handle the situation himself, and that is what works for a permanent cure. All the man needs is to feel that he is in control of the situation. If he can feel that, instead of fearing that the situation threatens to overwhelm him, then he sleeps. One might say that having self-confidence he does not fear to close his eyes.

HYSTERIA

HYSTERIA is not a disease. It is an indefinable state of mind which is the result of a combination of inherent tendencies mediated by difficulties of environment during the early years of life. There is perhaps, however, one fundamental thing about hysteria that is true of the other psychoneuroses, namely, that there is a large element of apprehension common to all these states of mind. The common name for apprehension is fear. Fear has certain definite subjective symptoms; not altogether subjective either, since one of them, rapid thumping pulsation, is detectable by the examiner's finger.

The symptoms of fear, briefly stated, are, first of all, a sense of oppression in the cardiac region with immediately a rapid pulse, which is felt by the chest wall and is described ordinarily as palpitation. At the same time that this palpitation comes on a sense of gripping or thickness in the throat begins, induced perhaps by the aforementioned change in the circulatory system. This is ordinarily spoken of as "My heart is in my mouth." In scientific terms it is described as a definite symptom, the globus hystericus. There is a sinking sensation in the region of the diaphragm which perhaps has to do with the change of blood distribution; that is, a contraction of the splanchnics that comes on almost immediately. There is a sense of giddiness which is also probably a vascular phenomenon.

Other symptoms of fear are cold hands and feet, hot head, weakness of the knees, and general feeling of weakness and lassitude. These are some of the subjective sensations, the physical symptoms of fear or apprehension, and I think one is perfectly safe in saying that fear is always present in the psychoneuroses.

Just what this fear is, what its origin is, is a matter for speculation, but is certainly not determinable according to our present knowledge. Anyone who attempts to explain it has never observed it in the very young for instance, where it seems, beyond

the peradventure of a doubt, to be something inherent rather than anything to be explained by environmental conditions; that is, by things that we can observe, analyze, and understand. We can say that each individual is apprehensive concerning the outcome of the conflict that exists in all of us between the pleasure-loving, self-gratifying desires that are typical of the child and the more purposeful far-reaching teleologic motives of the adult; of the outcome of the conflict of which perhaps none of us are conscious unless we stop and carefully study ourselves, but a conflict which exists nevertheless. As I say, it may be that that is the cause for apprehension in the adult—fear lest the impulse to satisfy the desire for immediate pleasure overcomes the other motives by which the people among whom we live and we ourselves also judge our conduct.

Leaving for the present this subject of whence and why the fear, and accepting the fact that fear is present in the psychoneuroses, some of the symptoms of the latter become a little more understandable. The case I will show you today is one of those in which the predominant symptoms relate to the abdomen, and yet in which the other manifestations of apprehension are also detectable.

This woman, who is twenty-five years of age, has vomited for the past ten months. She has lost 70 pounds in weight; she vomits practically everything she takes into her stomach after a period of an hour or two. There is a certain amount of tenderness over the epigastrium which might lead to a suspicion of organic disease, but I think is nothing more than an exaggeration of the normal tenderness that all of us have in this particular region. Gastric analyses, analysis of feces, blood and sputum analysis, temperature chart—none of these things throw any light on the genesis of this condition. Everything is perfectly normal and yet the vomiting keeps up. There has just been a change of doctors, and the patient has shown new symptoms. For the past few weeks she has been manipulating her diaphragm in such an extraordinary way that it seems almost unbelievable. There are periods when she will keep it in almost a vibratory motion for as long as fifteen to twenty minutes at a time, moving

it through such an amplitude that it moves her whole chest, so that one can scarcely make out respiratory movement independent of this diaphragmatic "tremor," and yet such respiratory movement is present and is not hurried. There have been times during these past few weeks when instead of this rapid, fluctuating movement of the diaphragm the latter has been held in spasm in such a way as to force the abdominal contents downward and forward, giving an appearance of abdominal tumor. These motor phenomena of the diaphragm have been quite independent of the vomiting, and I have been able to stop them by electricity and suggestion. These are not means that I am proud to use in a case of this sort except as they help to establish the diagnosis. I would much prefer getting the patient to realize that motor control can be practised beneficially as well as in this pathologic manner; that is, the "tremor" and "spasm."

This woman's previous history is interesting, as it throws a light on the genesis of this functional condition. It is difficult to get anything about her early childhood, much as it is to be desired. In fact, the first that I can get begins with the onset of puberty, except that she says that her mother was one never to talk "such things" over with her daughters. So this girl went to bed one night when she was thirteen years old entirely ignorant of what was to happen, and woke up in the middle of the night terrified to find the menses established. She was so frightened that she dared not call out, but got up and vomited. She has vomited with every menstrual period since. She is a Roman Catholic and very religious. In other words, she has a very marked feeling relative to sin, and it can be assumed without question that this that had happened during the night came as a punishment for previous sins.

It is to be noticed as I talk to her and as she presents herself that she constantly grins in a silly manner, is quite affected, and fails to express in her conduct the seriousness of her condition. This is an entirely different silliness from that seen in dementia præcox, where the silliness is more as if the patient had some joke of which they alone were cognizant that they were enjoying. In this case it is more a self-consciousness. One might

say that she wished to minimize the seriousness of her condition. This is an important point in the understanding of an hysteric. It belongs among the phenomena ascribable to splitting of consciousness. If we could define it we would say something to the effect that she wished to impress the on-looker with the seriousness of her condition, but did not wish to appear impressed herself.

I have had many interviews with the patient, and she has never expressed an idea of seriousness connected with the vomiting. She has never expressed dissatisfaction at the failure to cure or relieve. This in itself is extraordinary when we remember that the patient has been vomiting for ten months.

The general neurologic examination is negative. The reflexes are normal. I have not made sensory examinations because I have not wished to saddle the patient with sensory disturbances; that is, I am afraid to make sensory examination in a case like this lest the patient should grow to feel that sensory disturbance is to be expected, and so develop some one of the bizarre anesthesias of hysteria. I have assumed that this is hysteria. You might well ask why I am justified in the assumption that anybody would punish himself as severely as this patient has.

Perhaps I must explain this last remark—"why anybody would punish himself." Hysteria is essentially a disorder from within out. By that I mean there is no outside influence, such as microorganisms, climatic, dietetic, that is responsible for the genesis of the condition. It is a condition of the individual entirely independent from the environment. I think it would not be going too far to say that if this particular individual were in an atmosphere of perfect health she would nevertheless develop pathologic symptoms. She would develop a picture of disease. This is something which I must repeat, because the understanding of this factor is absolutely necessary to any step toward the understanding of the neuroses. They are from within. I will not say that is equivalent to calling them psychogenic. At any rate, we can feel fairly safe in saying that if the psyche or mental state of the individual was not such as it is the neurosis would not be developed, no matter what the other factors are. At least to

that degree the neurosis is psychogenic, and if there is a true "within," that term can be applied best to the psyche.

It is very difficult to learn anything about this patient's attitude of mind. She meets every question with "What's that got to do with it?" or she laughs and turns her face away. This much, however, I have learned, which sheds some light on our problem. She has been steadily at work ever since her school days helping in the financial arrangements of the family. Her younger sister worked only a year before marrying. As these facts were recited it was obvious that the patient felt a distinct resentment against the younger sister for shirking the responsibility. There is an additional factor which is represented by the small solitaire diamond on the left ring-finger. One might say that if this patient had enough nerve to get married she would have done so; that is, she has the chance. There is a young man waiting for her. If she is resentful against her sister for marrying, we are justified in assuming that she would marry also if there was not some deterring factor. I have attempted to discuss marriage with her, but her attitude toward this subject is the same as that toward her sickness—an obvious attempt to minimize the importance of the question under discussion.

You may well ask what this has to do with eleven months of vomiting, and with the meager information at my disposal I can only remind you that the vomiting began with the first menstual period, and that she has vomited with each menstrual period since. No one will deny that there is a closer relation between menstruation and marriage than merely that indicated by the fact that they both begin with "m." Also, resentment is to some natures that which lends spice to life. To carry a grouch and to vent one's spite upon others is a form of enjoyment that we have all observed. Whether the younger sister associates the patient's illness with her own disloyalty to the economic needs of the family or not is immaterial. If the patient senses any such relationship, that is sufficient, and there is a certain amount of evidence that the patient blames her illness on the fact that she has had to work so steadily. Naturally, if the sister had not married, but had done her duty as the patient

has, the patient would not have had to keep her nose to the grindstone.

In arriving at the diagnosis all these factors must be taken into consideration, but what was more important was the fact that when I first took the case she promptly began the terpsichorean manipulation of her diaphragm, which subsided without marked obstinacy to electricity and suggestion. Vomiting is a function of the stomach; the stomach lies immediately below the diaphragm. I am certain that vomiting would be no more difficult to produce voluntarily than the daily diaphragmatic gyrations indulged in by the patient. I stated at the beginning of the hour that I was dissatisfied with the methods used to rid the patient of these diaphragmatic symptoms. My dissatisfaction was based on the fact that a permanent cure, if there is such a thing, would be much more desirable through the voluntary co-operation of the patient than by these other methods.

I had some experiences with the enlisted personnel in the army that demonstrated this fact very clearly. Several of the men were suffering from convulsions. These were reported to me, and I inquired of the soldier just how he felt when the convulsion was coming on. In a most sympathetic manner I suggested to him by questions that he was feeling that way now—persuaded him that he was feeling "light-headed," or "slightly nauseated," etc. From this it was a mere step to producing a convulsion. As soon as the convulsion was well under way I would slap the patient sharply once or twice in the face and tell him to stop. I would then give him a lecture, dwelling on the fact that he had voluntary control of these phenomena. In some cases, at least, it was apparent that the demonstration to the soldier's satisfaction that the control of the situation was in his hands relieved him of further needs in that direction.

These measures sound rough—perhaps they are, but there is a necessity of producing a definite effect, and I know of no better way. The effect justifies the means. Of course, one cannot slap a woman out of an hysteric vomiting. I made the effort, however, to put before her a picture of her reactions toward herself such as would enable her to see that she had certain

reasons for producing symptoms of sickness. Naturally, the idea is offensive to anyone that they are suspected of attempts of any sort to elicit sympathy. The hysteric is, because of his weakness, especially unable to reconcile himself to such an idea. He is the last one to admit that any of his symptoms could be for the purpose of excusing himself either to himself or to others for the failure to make good. I have not been able to get this patient to stop vomiting as I was to get her to stop the diaphragmatic motions. I have taken up the various factors that might affect her, dwelling upon the part of the history that includes the vomiting at the time of the first menstrual period, and emphasizing the fact that vomiting recurred with each succeeding period; emphasizing also the fact that this present long-continued attack began at the time of menstruation. It is my hope and expectation that gradually the interrelation of the various facts known and unknown in her mind will take place in such a manner as to lead her to no longer feel the necessity of keeping up this defense against the outer world. When this time comes she will stop vomiting. It may come as a result of a transfer of interest to something more compelling. It may come merely as a result of fatigue; the idea will have played out.

This vomiting is an hysteric phenomenon. It has kept up for ten months. The long duration of its continuance must not be allowed to speak against its hysteric nature in spite of the teaching that the pathognomonic characteristic of hysteric phenomena is their evanescence. The hysteric symptom is the particular reaction of the patient at the moment. It does not seem to me at all necessary that that reaction must change frequently. Consequently, I feel that the permanence of the symptom does not count against its being considered of hysteric origin.

Note.—The patient has been seen recently, three weeks after leaving the hospital. She is up and around, is very much better, and vomits but rarely.

CLINIC OF DR. ISAAC A. ABT

MICHAEL REESE HOSPITAL (SARAH MORRIS MEMORIAL HOSPITAL FOR CHILDREN)

ASTHMA IN CHILDREN

THE first case that I present to you this morning is a child, W. K., male, six and a half years old, who came to the hospital February 3, 1918, with the following history:

He has been suffering from frequent attacks of bronchitis, with marked dyspnea, associated with vomiting. The father thinks they are brought on by indiscretions in diet. The first attack, which occurred four years ago, followed upon eating a portion of an egg. The symptoms noted at the time were cyanosis and dyspnea, occurring at night, accompanied by great restlessness, nausea, and vomiting. It is thought that similar attacks occurred after eating fish. Both of these articles, therefore, have been excluded from the diet. The attacks, nevertheless, occur at intervals, coming on especially at night about a half hour after going to bed, and last about ten minutes. They are associated with coughing. At the end of the seizure the patient usually vomits. The dyspneic attacks occur frequently while he is at school. When the little fellow was six months old he had a severe attack of eczema. At three he had whooping-cough. The mother states that she herself invariably has a rash after eating strawberries or after some indiscretion in diet. The father, who is a physician, is in good health.

The physical examination of the chest shows an emphysematous condition of the lungs. The heart is slightly dilated to the right. The examination of the blood shows 85 per cent. hemoglobin; 4,670,000 red cells; 9400 white blood-cells, of which 53 are polymorphonuclear, 38 small mononuclears, 5 large mononuclears, and 4 eosinophils. Tuberculin tests are negative. The

x-ray examination of the thorax shows some increased calcification at the hilus. The right lung shows some striations extending out to the periphery, which probably indicate a chronic bronchitis.

The story contained in this case record is one that is frequently encountered. Numerous histories might be taken from the records of the hospital which would simply be repetitions of the foregoing. The history here cited is obviously one of bronchial asthma; and it is to this disease, particularly as it occurs in infancy and childhood, that I wish to direct your attention this morning. If time permits I shall read you some additional histories to amplify the clinical descriptions.

Asthma is characterized by attacks of severe spasmodic dyspnea which may be preceded, accompanied, or followed by a bronchitis of varying degrees of severity. In infancy the association of asthma with bronchitis is a very close one. In older children the disease presents quite another clinical picture which differs in no essential points from the asthma of adults.

So far as the age incidence is concerned, LaFétra tells us that in 3 cases the symptoms were noted at birth. During the first three months of life he noted 2 cases; from the third to the sixth month, 3 cases; and from the sixth to the twelfth month of life, 3 cases. During the second year he had 8 cases; from the second to the fifth year, 9 cases; and from the fifth to the twelfth year, 15 cases.

Not infrequently there is a familial occurrence of the disease. It is not uncommon to be told by the mother or father that several children are asthmatic, or to be informed that the disease has existed in some other member of the family.

It is important to emphasize the fact that the infantile asthma differs from the type that occurs in adults and older children. For this reason the disease is often unrecognized in infancy. I have not infrequently observed well-developed cases of asthma that were diagnosed as bronchitis or even as bronchopneumonia.

It is often stated that asthma is more common in boys than in girls. It occurs among children of all classes, particularly among the well-to-do, especially those with neuropathic tend-

encies. It may occur at any season. It is very frequent during the fall and winter, when grip and bronchitis are prevalent, and it is also apt to appear in summer during the hay-fever season. It is interesting to note that children who are sent from severe winter weather into climates that are warm and dry tend either to improve markedly or at least to recover temporarily. I have in mind an infant who was suffering severely from asthma during the time that the family lived along the shore of Lake Michigan, who showed marked improvement after he had been removed to a home some five or six miles inland.

The effect of locality illustrates the capriciousness of the disease. Some patients do best in a dry place, while others avoid the ailment by living in a moist atmosphere. Knopf, who examined 5000 children at the Strassburg Polyclinic and found among them no cases of asthma, attributes the absence of the disease to the moist air of that region. To some patients the high locality affords relief, while to others relief comes only in a low region. In some the disease is relieved by remaining inland; in others, by dwelling at the seaside. It is noted at times that patients become asthmatic only when they visit a particular locality, and that at other times they are free from the disease only when they visit another particular locality. Sometimes an asthmatic patient can live on one street of a town and not on another. Health and disease may be a matter of living in different parts of the same house. Occupying one room the patient is free of asthma; in another, he succumbs to it. In short, it seems impossible to lay down any definite rule as to the influence of locality on the disease. It occurs everywhere, in all places and in all climates, in rural as well as in urban districts, in the mountains as well as at the sea level.

The same capriciousness is evident in the influence of the seasonal changes. One case grows worse only in winter; another, only in summer. It has already been stated that climatic conditions which predispose children to grippal infections and bronchitis also produce asthma. Almost in the same breath I may state that I have frequently seen children with severe attacks of the disease in the hot, dry spell of the summer,

when the dry heat produces new patches of eczema as well as asthma.

Much interest attaches to the exciting causes of asthma. As in most diseases which are of obscure origin, numerous hypotheses are offered as to etiology. There are some who believe that bacteria or their toxins may have some influence in the production of the disease. Koessler and Moody made an extensive study of the bacterial flora of the sputum of asthmatics. In 28 cases that they investigated they found, in addition to the aërobic organisms, the pneumococcus, streptococcus, influenza bacillus, Micrococcus catarrhalis, and certain anaërobic bacteria which they classified under three heads: "(1) A Gram-negative fusiform-like bacillus which produces a putrefactive odor in the culture, (2) A Gram-negative, very small bacillus which produces characteristic black colonies in the blood-agar, and (3) a very small streptococcus. These three organisms live in a certain form of symbiosis and are in every case present in the anaërobic tube."

The authors also state that they find a certain form of "asthma bronchitis due to the *tubercle bacillus* which can only be demonstrated by guinea-pig inoculation. Berkhart found tubercle bacilli in 5 cases. Others report similar findings."

It has been held that asthma may be the expression of an anaphylactic reaction to certain bacterial poisons; yet if autogenous vaccines containing the proteins which caused the anaphylaxis be injected, an attack of asthma does not follow. If the bronchial musculature in man acts the same as it does in a guinea-pig, a second injection of protein, even though it be small, should produce a spasm of the bronchial musculature, just as it does in the guinea-pig. This reaction, however, does not occur. Children, it may be said, are more apt to exhibit anaphylactic phenomena than adults. This increased susceptibility is due either to the greater absorptive power of the gastric mucous membrane in children, or to the acquisition of a partial immunity by adults.

The work of Talbot, Walker, Oscar Schloss, Goodale, Cook, and others have taught us that a certain group of children are susceptible to the toxic effects produced by eggs and other pro-

tein substances. These toxic symptoms are in the nature of anaphylaxis. Thus when a foreign protein is administered the body seems sensitized, and a subsequent dose of the same protein causes symptoms of anaphylaxis. Talbot tells us, however, that an injury to the intestinal mucosa is necessary in most cases before the reaction can take place, and that the greater the injury and the younger the infant, the more easily can the foreign protein pass through. It may be even assumed that in young infants the protein may permeate an intact mucous membrane. It is obvious, therefore, that sensitization can be most readily accomplished in early childhood. Thus an infant may be rendered susceptible to the toxins produced by proteins because of an inherited tendency to anaphylaxis; or it may become sensitized through an insult to the alimentary tract occurring either during the first days of life or late in infancy. It may be said, then, that in some infants and children asthma is a manifestation of anaphylaxis produced by protein substances which act as toxins.

I have frequently seen children in private as well as in hospital practice in whom attacks would be produced by the ingestion of egg-albumen. In one of the patients, a little girl of seven, who suffered from recurrent seizures of asthma, an immediate attack could be produced by ingesting the minutest portion of egg contained in cake, in bread, or in any other article of food. This child also responded to the skin test. If a minute portion of egg-white was placed on the skin, and the integument abraded with a scarifier, an intense localized urticarial reaction would occur in a few moments. It should be noted in connection with this case that a patient sensitive to one protein is very likely to become sensitive to others. In this instance the asthma would occur in response to a variety of causes. Other protein substances were capable of producing an attack, such as pollen of plants, nuts, and the emanations from certain animals. Milk may occasionally affect certain individuals in the same way.

It should be noted that the foreign protein may enter the body in various ways. It may pass through the mucous membrane by inhalation, by ingestion, or by autolysis of bacterial proteins coming in contact with mucous surfaces. The method

of entrance by inhalation may be seasonal or perennial. Seasonal inhalation, or hay-fever, produces symptoms at a definite time, coinciding with the flowering of special plants; while in perennial inhalation the exciting protein enters the body at any time and may produce asthmatic attacks. The emanations from horses, dogs, and cats are examples of this variety. Patients who are sensitized to animal substances, such as epidermal scales, hairs of animals, or feathers of birds, may show a group of symptoms varying from rhinitis to a severe asthma. Asthma may be caused also by vegetable substances in which the exciting protein is other than the pollen; for example, flour, potato, face-powder, or powdered orris root.

Various substances, such as fish, eggs, milk, meat, grains, cocoa, or nuts, may produce symptoms which vary from tickling in the throat to urticaria, asthma, or eczema. There is also a form of vasomotor disturbance in which the protein is bacterial. Walker has shown in examining the sputum of asthmatic patients that a diphtheroid organism is often found, and that the Staphylococcus pyogenes aureus is of very frequent occurrence. Whether these organisms act directly by producing irritation and inflammation of the mucous membrane, or indirectly by liberating protein substances which may be absorbed as foreign albumins, has not been definitely settled. If it can be affirmed that definite sensitization to micro-organisms exists, it is obvious that the use of vaccines would be valuable in treatment.

Relation of Asthma to Exudative Diathesis.—A group of clinicians, foremost among whom is Czerny, have attempted to explain a certain clinical entity under the caption of "exudative diathesis." It is known clinically that asthmatic individuals, particularly children, may suffer not only from disorders of the bronchi, but from other organs as well. On the basis of clinical observations, it is attempted to establish a connection between asthma and exudative processes, such as eczema and urticaria. Czerny defines the exudative diathesis as a change in the chemistry of the organism which is caused by a congenitally low tolerance to fat. In considering exudative diathesis as it affects the respiratory tract, he compares it to measles. This

latter disease produces an exanthem and an enanthem. The exanthem may be compared to eczema; the enanthem, to the catarrhal symptoms of nose, throat, and bronchi which occur so commonly in exudative diathesis. Continuing, he says that if an infant shows neuropathic tendencies or is hyperexcitable, the mild picture of bronchitis will be substituted by the more alarming condition of asthma. Again, comparing asthma to affections of the external skin, he believes that the same nervousness which tends to produce asthma will produce the intense itching in an eczema; whereas, in the absence of nervousness, a mild eczema without itching is nearly always observed. Czerny then proceeds to prove his hypothesis by diminishing the amount of milk in the food and by abolishing eggs from the diet.

It will be said at once that this clinical conception of exudative diathesis is not based upon experimental proof, that it is merely a speculation, and while it serves as a working hypothesis for carrying out certain lines of treatment, it has no foundation in pathology. Like all hypothetic considerations, however, it is useful as a temporary classification and serves as a basis for treatment. It is to be doubted whether it will have a permanent place in nosology.

It is possible that many of the obscure, irritative coughs without ascertainable physical signs depend upon an itching condition in the throat similar to that which occurs on the skin as a result of eczema. Similarly, pseudocroup may be the result of an angioneurotic edema.

Relation of Asthma to Other Diseases.—*To Spasmophilia.*—R. Lederer[1] calls attention to this form of bronchial spasm. In children suffering from spasmophilia the bronchial muscles are frequently subjected to tonic spasm, as a result of which there seems to be closure of the bronchi, more particularly of the smallest branches which communicate with the alveoli, causing a closure of the minute air vessels. In consequence, the alveoli collapse and atelectasis occurs. This condition may occur alone or may be associated with other constitutional manifestations of spasmophilia. One may conceive it as being analogous to the

[1] Zeitschrift für Kinderheilkunde, vol. vii, p. 129.

edema which occurs in association with the carpal and pedal spasm in tetany, *i. e.*, an edema of the bronchial mucosa. Or, indeed, it may be assumed that free fluid is poured into the lumen of the bronchi.

Concerning the frequency of this variety of bronchial spasm we may quote Lederer's figures: 5903 cases were treated in the hospital and 767 in the dispensary during one year. Of this number, 58 cases of spasmophilia that came under observation. The youngest patient was two months, and the oldest three years. Of these 58 cases, 6, or about 10 per cent., showed spasmodic symptoms of the bronchial musculature. These children responded to the electric tests and the Chvostek and Trousseau signs characteristic for tetany. Of the 6 cases which Lederer reports, all terminated fatally. The children all showed the typical symptoms of tetany, such as laryngismus stridulus, carpopedal spasm, Chvostek sign, and an increased electric excitability.

The condition of these children is typical. The breathing is labored and gasping; the alæ nasi dilate, and there is marked retraction of the ribs and sternum. Physical examination shows dulness over the posterior portion of the thorax which extends forward into the axillæ. Over the anterior portion the resonance is almost tympanitic in character. The lower margin of the lungs have descended, and the heart dulness is almost obscured by lung resonance.

Over the dull area, posteriorly, bronchial breathing is heard; anteriorly, vesicular breathing is elicited. The temperature varies from 100½° to 102° F. The condition remains unchanged for about three days. On the third day the cyanosis is extreme. The breathing is accelerated and noisy and may be heard at a distance. Over the dull area numerous small and middle-sized râles may be heard, and with increasing cyanosis, dyspnea, and cardiac weakness, death usually takes place.

At other times children may show manifest rickets, with gastro-intestinal symptoms and moderate spasmophilia. For several days there may have been indication of bronchial spasm, as shown by the severe dyspnea, dilatation of the alæ nasi, re-

traction of the thorax, and loud respiratory sounds. Eventually an attack of laryngismus occurs which is severe and protracted, and usually terminates fatally. Occasionally the attacks show interruptions. They tend to repeat themselves with the manifestations already referred to. Eventually symptoms of asphyxia occur, leading to a lethal result.

The diagnosis presents great difficulties, especially as between a bronchial spasm and a pneumonia. The explanation of the dulness which occurs posteriorly in these cases has been shown to be due to an atelectasis of the lung tissue. The *x*-ray examination tends to assist markedly in the differentiation. The picture lacks evidence of infiltration which characterizes a pneumonia. It shows well-circumscribed shadows between which dark tissue is situated.

The cases which have come to autopsy have shown characteristic pulmonary atelectasis. The posterior parts of the lung are of a dark bluish-red color, the surface is smooth and shiny, and the consistency is increased. The bluish-red color may involve an entire lobe or may be limited to smaller areas. In the regions which have not collapsed a vicarious emphysema is observed. The location of the atelectatic areas corresponds with the region which was dull upon percussion.

The microscopic examination shows that the walls of the alveoli have collapsed and lie close together and that the lumen has been obliterated. The contained cells have the character of normal endothelium. The blood-vessels show an increased content of blood, but nowhere is there any sign of active inflammation. Round-cell infiltration, which would indicate a possible pneumonia, is entirely absent. The bronchi show normal epithelial structures and no inflammatory secretion in their lumen.

The disease manifestation depends upon a spasm of the unstriped muscles of the bronchial tubes. It may be compared to the condition which causes carpopedal spasm. Owing to the spasm, the lumen of the bronchi becomes obliterated, and the communicating alveoli are cut off from their air-supply. Since these conditions may last for hours, days, or even longer, the

contained air is resorbed, the alveoli collapse, and their walls come in contact. In other words, the lungs become atelectatic. The atelectasis may occur either in small areas or be diffusely spread over a considerable portion of the lung.

Lederer considers this condition distinct from asthma, principally because it begins differently, and also because it remains uninfluenced by the administration of adrenalin. On the other hand, the differentiation of bronchotetany and asthma is not so simple a matter as Lederer would have us believe. Bronchotetany has many more points of resemblance to asthma than it has to bronchopneumonia. The most characteristic sign of bronchotetany is the extreme dyspnea. A large part of the bronchial musculature is in severe tonic spasm, so that the entrance of air and oxygen into the lung is prevented. The occurrence of atelectasis is a secondary affair, due to the bronchial spasm. It is also true that mild forms of bronchotetany may occur, involving smaller portions of the lung, with less extensive atelectasis.

It is a well-known fact that asthma occurs in two forms: first, the genuine asthma, which is not found frequently in young infants; and secondly, an asthmatic bronchitis. The first form—*i. e.*, the genuine asthma—may present the same symptoms as the bronchotetany without the extensive dulness. On the other hand, it is not conclusively shown that the asthmatic bronchitis may not in some instances depend upon spasmophilia. The important point is that a clinical asthma may occur on the basis of spasmophilia.

Asthma Associated With Nasal Lesions.—It is maintained that nasal lesions, such as occur, for example, in ethmoidal disease, are capable of producing asthmatic attacks. It has been shown experimentally on animals that if the posterior portion of the nose be stimulated, the lungs become dilated and rigid. If, on the other hand, the same mucous membrane be cocainized, this condition in the lungs disappears. As a general rule, the observation holds good in children that asthma is usually preceded by bronchitis, which, in turn, is preceded by an acute rhinitis. As a result of the progress of the catarrhal

infection, a spasm of the bronchial muscle takes place followed by the perverse type of breathing.

Attention has been called in recent publications to the possible relation of asthma to rachitis of the nose. As yet, however, nothing definite is known about this condition. By observation of the noses of rachitic children it has been pointed out that the condition occurs at the point where the cartilage and the small bones of the nose come in contact. In the rachitic nose the small bones undergo the same changes and show nodes similar to those which are observed in the ribs. They may also show a condition of subluxation. In nasal rickets, moreover, the mucous membrane shows a chronic cell infiltration.

It is reported by careful observers that nasal rickets is often complicated by bronchial asthma. The reflex neurosis producing the asthma may originate from any part of the mucous membrane, but particularly in the hyperemic area covering the rachitic nasal bone. It may be remarked incidentally that the nasal changes of rickets may be very pronounced when other manifestations are minimal or poorly developed, or when all other signs are wanting.

Walb[1] relates a typical case: A girl of eight years came to him with diffuse bronchitis, dyspnea, and definite symptoms of asthma. In the mucous membrane of the nose and the nasal pharynx a chronic catarrhal inflammation was found. These bones were deformed; the tonsils were hypertrophied; the teeth were markedly rachitic, and slight scoliosis was present. There were also large adenoid vegetations. After the removal of the adenoids and tonsils, the asthma still continued. In view of the suspicion of the rachitic condition of the nasal bones, the child was placed on an appropriate diet, and phosphorus and cod-liver oil were administered. She eventually made a recovery.

We may also in this connection refer to Kassowitz, who, up to the present day, has been the foremost student of rickets. He considers that asthma is in some way or other a complication of rickets, though he makes no reference to the nasal origin. He

[1] Rachitis of the Nose and Its Relation to Asthma, Deutsche Med. Wochenschr., 1913.

records a case of a markedly rachitic child, fourteen months of age, who presented loud bronchial râles and marked dyspnea. Under treatment with phosphorus and cod-liver oil the patient promptly recovered not only from the rickets, but from the asthma as well.

Other Diseases in Which Symptoms of Asthma are Present.—Enlarged bronchial glands may give rise to severe dyspnea which may simulate bronchial asthma. In young infants an enlarged thymus may cause a varying degree of dyspnea, which may also suggest an attack of bronchial asthma. In the more severe cases of thymus compression there are symptoms of tracheal stenosis, with retraction of the epigastrium and the upper portion of the sternum. Cyanosis is a common symptom. The enlarged thymus can be demonstrated by a physical examination and by the *x*-ray.

Asthma of cardiac and renal origin requires no special consideration at this point.

Symptomatology.—Asthma may occur in children at almost any age. Clinically, we may recognize two main varieties: first, those cases which are associated with bronchitis; and secondly, those which are characterized by sudden onset, usually accompanied by pulmonary emphysema, and in which there is a tendency to periodic recurrences. In the first form the disease begins with marked bronchitis, fever, lassitude, rhinitis, restlessness, and even delirium. Anorexia and vomiting may occur. Fever may reach a considerable degree. The pulse is frequent. The dyspnea, however, is the most characteristic symptom. Respirations may be 50 to 80 and even higher per minute.

The dyspnea is usually expiratory in character. The breathing is loud and noisy. The inspiration in most cases seems somewhat more free and less obstructed than the expiration, which is longer and whistling in character. If one inspects the thorax, he is struck by the immobile appearance of the chest during expiration, a condition resembling the emphysema of adults. The cough is usually persistent and disturbing; the breathing continues noisy. One has the feeling that there is considerable secretion. The younger children, however, do not expectorate it. If

the patients vomit, mucus may be seen in the vomited material. If the chest is examined, one hears numerous dry, whistling, sibilant râles. Sometimes percussion reveals an emphysematous character of the lungs. In infants the possibility of a capillary bronchitis should be considered.

The following case illustrates the condition as described above:

A. C., male child, age eight months, was admitted to the hospital because of dyspnea, cough, fever, and prostration. About four days ago the mother noted that the respirations became rapid and jerky, and the child had great difficulty in breathing. At times he became cyanotic. The respiration was wheezy in character, so that it could be heard at a considerable distance. The infant had been coughing for two weeks, during which time the cough had been non-productive, though the condition had become more severe during the past forty-eight hours. For four days the little fellow was greatly prostrated. He lay in bed breathing very rapidly, crying feebly, and refusing food. He seemed more comfortable when propped up on pillows. The mother informed us that he had had an attack similar to this four weeks previously; that he had had frequent colds since his birth, although he had suffered from no definite illness. His respirations were 72 per minute; pulse 160; fever 102.6° F. The blood examination, among other things, showed 18,000 leukocytes, with 78 polymorphonuclears. The examination was negative except for his lungs, which showed normal boundaries and were somewhat hyperresonant. Upon auscultation, one could hear over the entire chest every variety of dry râle, which were loud and penetrating and seemed almost constantly present.

The patient was given $\frac{1}{1000}$ gr. of atropin and $\frac{1}{50}$ gr. of codein every three hours for four doses; was fed breast milk and orange-juice and a small quantity of cereal. In two days the temperature became normal. The cough abated; and in a few days the patient had made a complete recovery.

Another patient, T. O., five years old, female, came for examination because during the past year she has had frequent attacks of bronchitis, accompanied by dyspnea. These attacks recur every week or two. The manifestations are typical asth-

matic spells. The dyspnea is severe and continues the entire night. There is no definite relation between the attack and the ingestion of any particular kind of food. Her temperature is 98.8° F.; she weighs 41¼ pounds. Examination of the urine shows a trace of albumin and 10 to 12 pus-cells per field, with an occasional clump of pus-cells. The blood shows 18,000 leukocytes, of which 38 are lymphocytes, two large mononuclear cells, 47 neutrophils, and 13 eosinophils. On examination she presents a dusky appearance. Her thorax is slightly emphysematous; and on auscultation, one hears numerous whistling, sibilant râles.

Another child, male, age nine years, was admitted to the hospital because of recurrent attacks of coughing. These spells occur every winter at intervals of about a month and last from twenty-four to forty-eight hours. They are more frequent at night than during the day. During the attack the child coughs frequently, complains of pain in the epigastrium, becomes markedly dyspneic, is unable to lie in a recumbent position, and is more comfortable when propped up in bed. The anorexia is almost complete. His temperature is 101.6° F., pulse 124, respirations 40. The parents maintain that all these symptoms have been present since the child was four weeks old.

The examination shows that the child has a barrel-shaped chest; the breathing is labored; the chest is in the inspiratory position; the respiratory excursions are very limited and hurried; the breathing is harsh, with numerous dry râles. The respirations are wheezing in character. The father has had recurrent asthma for years. The blood examination shows 9900 leukocytes, 80 neutrophils, 16 small mononuclears, 3 large mononuclears, and 1 eosinophil. The von Pirquet test is negative.

The second type of asthma as it occurs in children resembles in many respects the asthma of adults. The attacks tend to be recurrent and are present in every degree of severity. In many of the patients there is a definite neuropathic history in the family. Many of them are particularly susceptible to changes of weather. Some are attacked mostly in the winter; some have their attacks in the summer, associated with hay-fever. In some instances the asthma bears a striking relation to eczema, thus presenting

the condition which has been described by Czerny as exudative diathesis. Others are susceptible to certain kinds of foods, such as proteins, etc.

As a rule, children who have apparently been in normal health are suddenly attacked with severe dyspnea shortly after retiring. There is little or no cough. The breathing is rapid. The dyspnea may be intense. The chief trouble is expiratory, the chest being in position of full inspiration, so that strenuous efforts are made by the expiratory muscles to empty it of air. In severe cases there may be marked orthopnea. Cyanosis of varying degrees of severity is usually present, while fever is usually absent. The symptoms in most instances may be explained on the basis of obstructed breathing in the bronchi, interferences with pulmonary circulation, and accompanying emphysema. In the recurrent and chronic cases the facial appearance is suggestive. There is a tinge of cyanosis about the face, particularly the lips, and a dilatation of the small veins of the cheek and conjunctiva. The hands are cool; the pulse is rapid, often tumultuous or small. Sometimes the patient has involuntary passage of feces or urine. The alæ nasi become large on inspiration. The sternal notch and the epigastrium are retracted, and all the accessory muscles are in lively activity. On percussion, the lungs are hyperresonant and the normal excursion is diminished. On auscultation, loud, whistling, and sibilant râles are heard, which almost obscure the normal respiratory tones.

The expectoration contains Curschmann's spirals, Charcot-Leyden crystals, and eosinophil cells. The duration of the attacks is variable, lasting from a few minutes to hours or even days. They usually disappear as suddenly as they come. Some children may be perfectly normal between the asthmatic attacks. Sometimes, even though the attack disappears, a bronchitis continues. Some children do not quite regain their normal health in between times. They continue pale, show a degree of lassitude, and are irritable. As a rule, the attacks tend to disappear in later childhood, though sometimes they continue late into adult life.

Our records contain numerous cases of asthma in children of all ages. Some of them are attacked only during the hay-fever

season and are relieved by change of climate. Some are susceptible to one or another kind of protein food; some, to animal emanations, and in some the condition is chronic and occurs apparently after slight colds, attacks of indigestion, nervous excitement, or without reference to any definite exciting cause.

An interesting case is that of J. M., female, age four years eleven months. She was delivered by cesarean section, the mother dying three days after the birth of the child. The patient has been artificially fed since birth. Since she was seven months old she has had eczema, which disappears and returns at varying intervals. Asthmatic attacks began when she was about twelve months old. At first they recurred at long intervals, but after she was two years old the periods became shorter and the attacks more severe. At three years of age the child acquired whooping-cough. The combination of this disease and the asthma caused intense suffering and produced attacks of great violence which were marked by cyanosis, dyspnea, and respiratory distress. The child became greatly exhausted. She was unable to recline in bed and had to be supported in the sitting position in the arms of a nurse most of the day and night. The dyspnea and the discomfort continued almost without interruption. The heart became markedly dilated; the pulse weak and rapid; the cyanosis increased, and numerous râles were heard over the lungs, though the heart tones remained clear. This combined paroxysm of whooping-cough and asthma lasted for days at a time. The cough itself persisted for weeks, during which time there was an occasional abatement of the asthmatic manifestations. The child eventually recovered from the whooping-cough. The dry, broken eczema on the skin, however, persisted, and the asthma itself, after intervals of several days' absence, would recur, lasting for two or three days at a time. The patient obtained great relief by a prolonged visit to New Mexico, though the asthma recurred upon her return to Chicago.

The examination shows the child with a dry skin, broken here and there by fresh eczema patches, and a slightly bluish discoloration of the visible mucous membranes. The tongue shows map-like configurations on the surface, presenting the condition

known as lingula geographica. Examination of the thorax shows some involvement of the accessory muscles of respiration even during quiet breathing. The urine shows no pathologic findings. The blood shows 85 per cent. hemoglobin, 16,200 leukocytes, 40 lymphocytes, 4 large mononuclears, 47 neutrophils, 2 transitional, and 7 eosinophils. Percussion elicits a hyperresonant note. The respiratory excursion is diminished and the lung tissue overlies the normal cardiac area. The lungs are emphysematous. Auscultation gives evidence of a moderate degree of chronic bronchitis even during the quiescent periods. During an asthmatic attack the sibilant and whistling râles predominate over every other sound.

The food was changed and adapted in every conceivable manner without in the least affecting the course of the disease. During a severe paroxysm drugs exerted, for the most part, little or no influence. The greatest relief was obtained, temporarily, by $\frac{1}{20}$ to $\frac{1}{30}$ gr. of morphin hypodermically. The case also represents the clinical findings which are described under the caption of exudative diathesis.

Another case is that of a boy who was brought to me when eight months old with a severe eczema on cheeks, forehead, and wrists, which itched intolerably, so that he was awake and restless night and day. He was having 1 quart of milk daily. This food was reduced in quantity; cereals and broths were substituted. In consequence, the eczema improved so that the itching disappeared.

At eleven months of age asthma appeared and has persisted up to the present. The attacks occur most frequently in winter; seldom in summer. They come on after an acute cold, though the mother observes that they will also occur after indigestion or great fatigue. They are very severe in nature and last two or three days. The patient has marked idiosyncrasy against egg. Even the slightest trace of it in his food will bring on an attack. He is now seven years old. The attacks still continue, though they occur at long intervals. He is undersized, of insufficient weight, eats poorly, and is still sensitive to egg.

My colleague, Dr. J. H. Hess, furnishes me with a brief refer-

ence to a very interesting case of food asthma in a boy eight years of age, the son of a physician. The boy was subject to recurrent attacks of asthma, of which the father was unable to ascertain the etiologic factor. They usually came on during the early evening and lasted for about six or eight hours, increasing in severity in the course of the night. After each attack the little fellow became perfectly normal.

In endeavoring to ascertain the causal factor the feeding history was carefully investigated. It developed during the inquiry that the father himself disliked pork, so that it was never served while he was at home. The grandmother, however, confessed that whenever professional engagements necessitated the father's absence from home, the mother usually indulged in a pork debauch. The grandmother suspected that this food had something to do with bringing on the attacks, for whenever the boy ate pork he was seized with violent asthma. Two weeks after the attack mentioned the boy was given a roast-pork dinner as a test-meal. During the ensuing night he was again seized with a violent attack similar to the preceding one, thus proving without doubt his sensitivity to this article of food. Naturally, it has been omitted from the diet, and, in consequence, he has had no further attacks.

Prognosis.—As has already been indicated, many of these children afflicted with asthma tend to recover before puberty. In some the condition persists into adult life. The prognosis depends largely upon the permanence of the emphysema. If the attacks are of infrequent occurrence and the emphysema slight, the prognosis is favorable. When the attacks are of frequent occurrence, and the emphysema becomes extensive and firmly established, a chronic bronchitis occurs. The patients show more or less cyanosis and a persistent dyspnea. They are in permanent ill health and are likely to succumb to pulmonary or cardiac complications. It should be emphasized again, however, that these are the exceptional cases. The great majority that have come under our observation tend to recover permanently. The attacks, however, may be replaced by other nervous manifestations in later life, the most common of which is migraine.

The differential diagnosis of asthma must be made from con-

genital stridor, thymic asthma, pseudocroup, diphtheria, laryngitis of measles, whooping-cough, retropharyngeal abscess, enlarged bronchial glands, and foreign bodies and ulcers in the larynx.

Treatment.—Prophylaxis. The treatment of asthma in children calls for a most careful physical examination. The presence or absence of rickets, spasmophilia, disease of nose or throat, the presence of eczema, neuropathic taint, or an inherited disposition to the disease—all may have importance in the treatment.

In 1907 Besredka stated that calcium chlorid has the power to prevent anaphylaxis. Since then this discovery has been confirmed experimentally by others and has proved effective in preventing the occurrence of attacks. It is used in cases of spasmophilia in infants and in children of every age. It may be given for a long time with occasional intermissions of a week or two. Young infants of a year or less may be given 3 to 5 grains in watery solution four times daily.

In older children respiratory exercises are of value in connection with other hygienic measures, such as daily bathing, cool sponging, and a life out of doors. Patients should eat carefully and provide for a daily evacuation of the bowels. They should be spared nervous overstrain both at home and at school.

For the hay-fever patients relief is frequently obtained and tolerance increased by injecting pollen extracts derived from the special exciting plants. Goodale directs that the pollen be either placed in a solution for extraction or preserved dry for an indefinite period. A suitable extract constitutes a stock solution from which subsequent dilutions may be made. In order to determine the strength of the solution to be used for injection a skin test should be made. It should be stated, however, that in children under ten years of age who present well-defined symptoms of hay-fever, no skin reaction with the prevailing pollen will take place.

When possible, however, the special exciting pollen should be determined by the skin test. The initial dose of the injection should not exceed 5 to 10 drops of the aqueous extract of the pollen. The dose may be gradually increased drop by drop thereafter. Injections should be made at intervals of two days

to a week, and should in most cases be stopped before the date of attack, since the introduction of protein may cause an increase of symptoms at this time.

In cases where asthma occurs suddenly during hay-fever, removal to the mountains or to northern resorts gives prompt relief and is to be advised.

The local treatment of the nasal mucous membrane should be undertaken in every case where a pathologic condition exists. A normal nasal mucous membrane is less likely to absorb the specific protein than a diseased one. For this reason nasal polypi —chronic ethmoiditis—should receive prompt and appropriate attention, preferably by a specialist.

Treatment of the Attack.—Adrenalin solution in 1- to 2-drop doses of a 1 : 1000 solution frequently checks the attack. At times injection of morphin in doses of $\frac{1}{20}$ to $\frac{1}{60}$ gr., combined with $\frac{1}{1000}$ gr. of atropin, is required to control the paroxysm. Talbot has also suggested that in order to build up immunity against sensitizing proteins, children who show anaphylactic reaction to egg-albumen should be given minute doses of this protein, preferably in capsules, increasing the dose until the patient is immunized. Treatment by the use of autogenous vaccines has also been recommended. Where there is secretion from trachea or bronchi, the organisms are obtained by aspirating the secretion, isolating the organisms, and preparing the vaccines from this aspirated material. Although I have seen this method tried, I have never been convinced of its efficacy.

During the attack I have frequently seen temporary relief obtained by burning nitrate and stramonium papers. If everything else fails, the little patients receive the greatest benefit by a change of climate. I have frequently seen children for whom life was intolerable during the northern winter, who improved almost at once when removed to Arizona or New Mexico. Sometimes relief is obtained for these patients in Florida or California, though experience in each individual case determines the best locality. The hay-fever patients are relieved by removal to northern or mountainous regions, or occasionally by a sea-voyage or by trips to the sea-coast.

CLINIC OF DR. MAXIMILIAN J. HUBENY

CHICAGO POLICLINIC

ROENTGEN EXAMINATION OF THE APPENDIX

THE appendix is probably the worst maligner in the human race. While acute appendicitis presents certain difficulties in diagnosis, the chronic form is many times unrecognizable. From the roentgenologic viewpoint little need be said of acute appendicitis, except that occasionally one might be illumined in a left-sided appendicitis, several such cases having been reported. In such an instance an opaque enema, carefully given during fluoroscopic examination, will show if we have a case of transposition. It is a well-established fact that if a patient has once had appendicitis he will always be liable to suffer from another attack if the appendix has not been removed.

The function of the vermiform appendix seems to be in doubt; some regard it as a vestigial organ, stating that the vermiform process in man is the degenerated remains of the herbivorous cecum, which is associated with a large appendix, while the carnivorous cecum has a relatively small appendix. Others (Robinson) state that it secretes certain hormones which are quite necessary to stimulate the cecum, thereby provoking its contractions and expediting the issue of the feces collected. Keith's New Theory of the Causation of Enterostasis and the Theory of Sphincter Zones as the Pace-makers of Intestinal Peristaltic Activities advances the thought of a ceco-appendical plexus zone. It is considered that normally there is an intimate co-ordination in the rhythm of each successive segment of the entire intestinal tract, and that any disturbance, irritative or inflammatory, upsets this rhythm with reflex manifestations in the form of spasms. Thus, given an irritative lesion in the appendix, reflex spasm

occurs, and if permitted to continue over an extended period there is a progressive weakening or atony of the circular muscle-fibers which provokes an enterostasis. Such a view has recently been advanced by Ochsner. He states that clinical observations become more and more convincingly certain that the appendix possesses a peculiar neuromechanism which normally is exercised in the designed functional activities of the ileocecal region.

The foregoing remarks are made because of the desirability of determining whether we are dealing with a normal appendix or a diseased one. There should be no hesitancy of ablating an inflamed appendix; because of atypical symptoms it is often removed and found to be uninvolved, while the condition of the patient remains as heretofore. The appendix has frequently been removed when the real cause of trouble was a stone in the urinary tract, especially in the lower right ureter; tuberculous peritonitis, tubercular mesenteric glands, painful right inguinal hernia, pleurisy, pneumonia, cholecystitis, or disease of the tubes and ovaries.

It is an acknowledged fact that the cecum is grossly classified into four groups and that its location is variable. The appendix has a different point of relative origin in each type. This brings up the issue of McBurney's point, which exemplifies the acceptance of an opinion based on the law of average. Surgical interventions, postmortems, and roentgenologic examinations concur in the occasional instances of an unusually placed cecum and appendix. It is readily apparent that any method not associated with any hazards should be accepted as a diagnostic aid.

The object of this paper is to place confirmatory data in our hands, which, with other clinical findings, warrant a diagnosis of chronic appendicitis.

Holzknecht, Albers-Schoenberg, Beclere, Jordon, Groedel, Riedel, and other European roentgenologists did some early work on this subject; however, considerable credit must be given some of our American collaborators, notably Cole, Quimby, Imboden, George, and Case, for appreciating the possibilities of this method of examination.

There are two methods of visualizing the appendix: the first is by injecting an opaque enema; the second by the ingestion of an opaque meal. The second is preferable because of the greater frequency with which the appendix can be demonstrated. In examining the patient the fluoroscopic method is the most satisfactory, and this should be done in the vertical and horizontal positions.

By proper manipulation an otherwise hidden appendix can be shown; also movability and relationship to the surrounding structures noted. The plate method should also be used, for it occasionally gives additional information. Sometimes stereoscopic plates are indicated whereby one can trace a retrocecal appendix, or an appendix in close proximity to the cecum or ileum, which might otherwise be overlooked.

It is necessary that the lumen of the appendix be patent. The appendix may not be demonstrated if its lumen is obliterated, or if adhesions or kinks are present near the proximal end; or if an acute attack exists the infiltrated mucous membrane prevents the entrance of the opaque substance. Also an enterolith or previously contained matter may prevent its filling.

The writer has had the experience in several cases in which the first examination failed to reveal the appendix, but a second examination disclosed its presence.

The two possible factors in filling the appendix are antiperistalsis in the ascending colon and sedimentation.

Groedel has recently asserted that every appendix which permits the entrance of an opaque meal is pathologic. However, the more rational assumption is that if the appendix empties itself at the same time that the cecum does, it should not be considered diseased, for Moro has cinematographically demonstrated peristalsis in the appendix of a dog similar to that which exists in the cecum. Cohen says that cecal contents normally enter the appendix; it should, however, be empty when the cecum is empty. He states it may fill and empty itself several times during the same opaque meal.

The time of examination is important, for the appendix commences to fill shortly after the cecum. This is usually after

six hours, although there are cases that fill earlier. From this time on until the bowel is empty, and often for several days afterward, the appendix remains visible. Pirie has reported one case in which the shadow persisted for forty days.

Pathologists inform us that the evidences of previous appendical inflammation are peritoneal adhesions, obliterations of the whole or portions of its lumen; strictures of the lumen with more or less dilatation distal to it, and lastly, the presence of hard concretions which are retained by strictures or produce the same effects as strictures.

Concretions may occasionally be shown. The other factors are inferential from the following information: The visualized appendix with fluoroscopic manipulation will give us: (1) the size, including the length and calibre; (2) position and direction; (3) drainage; (4) mobility; (5) kinks; (6) the location of applied pressure to visceral topography. This latter point is quite important, for should pain be constantly elicited by pressing on the appendical shadow, one is justified in suspecting its involvement, for seeing palpation is more valuable than palpation without seeing. Crane has stated that if a constant point of tenderness located on the cecum approximating the site of the appendix be elicited, even though the appendix is not visualized, it would justify the conclusion of an inflamed appendix.

In palpation great care must be exercised, for if too vigorous, traumatic sensitiveness might be produced, thereby misleading one into concluding that the pain or sensitiveness is inflammatory. This is quite important, and if appreciated will reduce the possibility of error. This often throws light on cases in which anomalous symptoms have resulted from the appendix being situated in the pelvis, behind the cecum, or unusually high, when the symptoms may simulate gall-stones or duodenal ulcer or vesical involvement.

Fluoroscopically the presence of adhesions in connection with the appendix, terminal ileum and cecum, whether to each other or the surrounding parts, can often be recognized, especially if they are extensive. If the cecum is in the pelvis it can often be drawn into the right iliac fossa. When this cannot be

done, it is impossible to determine whether adhesions are present, as the cecum and appendix are too deep to be palpated satisfactorily unless the colon is distended with air or the bladder is not emptied for ten or twelve hours; sometimes the Trendelenburg position releases a mobile cecum so that the appendix is palpable and visible.

The appendix produces effects on remote organs. The stomach may be hypertonic, so that it empties itself rapidly. This is much less frequently observed than with duodenal ulcer. More commonly a spasm occurs in the center of the stomach. Indeed, chronic appendicitis is, after gastric ulcer, the most frequent cause of spasmodic hour-glass constriction of the stomach. Sometimes pressure over the appendix will produce a spasm; in most cases epigastric discomfort was simultaneously produced. Barclay declares that appendicitis causes an impairment of the ileopyloric reflex, producing appendix dyspepsia. Occasionally we have associated a delayed pylorospasm. Intestinal stasis is sometimes the result of adhesions following a chronically inflamed appendix.

Stasis of the cecum and ascending colon is often due to reflex inhibition resulting from chronic appendicitis. In such cases the cecum and an ascending colon are often abnormally large and unusually mobile.

Enterospasm, usually affecting the proximal half of the transverse colon, is sometimes present.

When the appendix hangs over the brim of the pelvis, or when the cecum as well as the appendix is situated in the pelvis, chronic appendicitis may produce dyschezia (Hurst).

CLINIC OF DR. HENRY F. HELMHOLZ

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PYELITIS IN THE NEWBORN

PYELITIS in infancy has been emphasized by practically all writers on the subject as one of the most frequent causes of obscure fever. Most observers are agreed that the condition is relatively more frequent among baby girls than among baby boys. As regards pyelitis during the first few weeks of life the literature is singularly barren. Only a single publication by Kovalesky and Moro[1] was found. They described 2 cases of pyelitis in the newborn. The youngest of the two was a weak, subnormal boy of eight days, whose urine contained a large number of pus-cells, blood, and albumin. Culture taken from the urine showed the presence of a Bacillus coli. The illness terminated on the eleventh day as the result of a Bacillus coli septicemia. Von Reuss, in his book on The Newborn, thinks that pyelitis is probably more frequent in the newborn than in the older infant, because of the frequency of generalized infections in the first few days of life. He says, however, that clinically the evidence for this fact is still lacking.

In view of the relative infrequency with which cases of pyelitis have been described in the newborn, it seemed of interest to describe 3 recent cases of pyelitis that have come under the observation of my associate, Dr. Sauer, and myself. Contrary to the general rule that pyelitis in infancy is more frequent in baby girls than in baby boys, these 3 cases are all in boys. The diagnosis of pyelitis was made in one case on the sixth day, in the second case on the tenth day, and in the third case on the

[1] Kovalesky and Moro, Ueber Zwei Fälle von Koliseptikäme bei Neugeborenen., Klin. therap. Wochenschr., 1901, No. 50.

fifteenth day. In each instance the diagnosis was made the first time the child was seen, so that it is difficult to say in each instance how long the condition had existed beforehand. In all three cases it is probable that the pyelitis had existed for some days before its discovery, because the urinary findings were those of a well-established case of pyelitis. In all the cases there was nothing in the symptomatology of the physical findings that would have led one to suspect a pyelitis, unless it were the absence of anything to explain the fever in the first two cases. The diagnosis in each instance was the result of urinary examination.

Whether we have been overlooking cases of this kind in years gone by, or whether it is one of those peculiar coincidences in medicine that we should have seen 3 cases of this kind in a period of six weeks, it is difficult to say, but it can be said that these are the first cases in the newborn that we have seen in ten years of practice.

The 3 cases in detail were as follows:

CASE I.—Baby boy S. was born November 13, 1917, with a birth weight of 9.6¼ pounds. The child lost considerable weight during the first twenty-four hours; its weight being only 8.6 pounds on the second day. The following day it developed a temperature of 103° F. and the weight dropped to 8.3 pounds. For a period of about a week its temperature continued normal, and the child's weight remained stationary on a combination of breast milk and modified cows' milk. On the 23d it was circumcised, and three days following the temperature again went up. The weight now dropped to 7.15 pounds. The temperature varied from 97.6° to 103° F. The bowels, which had been kept open with almost daily doses of oil, became very loose and frequent. On the 29th and 30th the temperature varied between 100° and 104° F. The stools remained green and the child was in a very critical condition, cyanotic skin, turgor poor, marked tympanites. On December 1, 1917, the child's temperature was 102.4° F.; the stools were loose, green and watery, and child appeared to be suffering from an acute gastro-enteritis. At the first examination the child was catheterized and a small amount of turbid urine was ob-

tained containing a large number of pus-cells; marked positive test for albumin, and on culture yielded a pure culture of Bacillus coli. The weight on this day was 7.11 pounds. The child was put on 5 grains of sodium bicarbonate and 5 grains of sodium citrate every three hours. Water was forced by mouth and saline solution given by rectum. Albumin-milk (1½ ounces) was given every three hours by mouth. The following day the temperature remained at 102° F. and the weight dropped to 7.9 pounds, but with the increased amount of fluids the child seemed somewhat better. During the next three days the temperature still varied between 99.8° and 102.4° F. Urinary examination: Albumin +++, pus-cells +++, red blood-corpuscles +, hyaline and granular casts +. On the 4th of December urine was alkaline, contained a trace of albumin, pus-cells +++, and an occasional red blood-corpuscle, but no casts. On December 12th the temperature was normal. Albumin-milk had been increased to 3 ounces and the weight was gradually increasing. On the 7th there was still a trace of albumin and ++ pus-cells in the urine. From that time on the child continued to gain. The pus-cells in the urine gradually subsided, and by January 1, 1918, the urine was practically normal. Since that time repeated specimens of urine have been obtained, all of which have shown practically normal findings.

Case II.—Baby boy S., born December 5, 1917, with birth weight of 8.14 pounds. Child was born at the Evanston Hospital, where it remained four days. Child was breast fed every four hours. Child was doing well at the breast, keeping its food down and sleeping well at night. Stools had rather typical hunger-stool appearance. There was a slight infection of the cord when seen for the first time on December 15th. Temperature was 102.5° F. The urine on that day was strongly acid, albumin +, pus-cells +++. Gram-negative bacilli were found in pure culture. The temperature continued to run between 97° and 103° F. Abdomen was rather tense. There was no vomiting. December 18th, 19th, and 20th temperature varied between 97° and 102° F. The urine was now alkaline; pus still present +++. Culture showed pure culture Bacillus coli. The temperature on the 22d became nor-

mal and has remained so ever since. The urine contained pus until February 1st, when the urine became entirely free from pus. The child was fed on a mixture of albumin-milk and water, half and half, 3½ ounces, six times a day. On the 12th of January the weight had returned to 8.7 pounds; on the first of February, to 9.8 pounds. Specimens of urine obtained on several occasions after this showed a perfectly normal urine. On the 7th of March the child weighed 11.3 pounds, and was gaining on a simple milk dilution mixture.

CASE III.—Baby boy B., born January 2, 1918. Normal birth. For the first twenty-four hours seemed perfectly normal. After that time had some difficulty in retaining its food. Birth weight 9.1 pounds. Temperature after the third day ran slightly above normal, on one occasion reaching 100° F. The case was seen for the first time on January 7th, at which time the weight was 9.1 pounds. The child was still regurgitating slightly, but the bowel movements were normal. It was receiving six feedings at the breast. Physical examination was entirely negative. Examination of urine showed +++ leukocytes, + red blood-corpuscles, and culture of urine showed pure culture of Gram-negative bacilli. Except for the fact that the temperature was slightly above normal the child showed no symptoms whatsoever. The child was given 10 grains of sodium citrate, well diluted in water three times a day. Two days later the temperature returned to normal and has remained so ever since. The regurgitation continued, but with that exception the child made an uneventful recovery.

As is seen from the histories, all 3 cases were in boys, and in all 3 cases a colon bacillus was isolated in pure culture. In the one instance, Baby B., in which the diagnosis was made on the sixth day, there was practically nothing in the history of the case or in the physical examination that might explain the source of the infection. We have a case of pyelitis in an otherwise perfectly healthy boy baby, weighing 9.1 pounds at birth. In the second case as a possible source of infection we have an infected navel. Unfortunately, cultures were not taken from the navel, but in all probability the infection was with a member of the coccus group

rather than the Bacillus coli. This corresponds to our experience in older infants, in which, when pyelitis complicates an infection of the tonsil, skin, or other organ, the infecting organism is usually the Bacillus coli and not the organism found in the original infection. The third instance is the one in which the child was circumcised. The fact that the pyelitis developed shortly after circumcision makes it seem possible that the operation had something to do etiologically with the pyelitis. The toxic condition that this last infant was in when seen for the first time was probably due to the pyelitis primarily, and the nutritional disturbance probably secondary to the pyelitis aided in its production. It is striking that these 3 cases and the one reported by Kovalesky and Moro were all in boys. The ease with which an organism passes through the intestinal wall in the early days of life make it seem probable that the organisms gained entrance from the bowel and were carried to the kidney by way of the blood-stream.

The symptomatology, as is usual in these cases, shows wide variations, and practically nothing was seen clinically that would call attention to the urinary tract. In two instances there were practically no symptoms, and in the third case the symptoms which were observed were of the gastro-intestinal canal. The clinical picture of none of the 3 cases was suggestive of a probable pyelitis. In all three instances there was a slight rise of temperature; in the one instance never above 100° F., in the other two up to 102° and 104° F. As is so frequently the case in pyelitis of older infants, in Case I the gastro-intestinal symptoms completely dominated the symptomatology, and until an examination of the urine was made the child was supposed to be suffering from an acute gastro-enteritis. The rapid recovery after the institution of the treatment and the increase in weight after the second day of treatment are strongly in favor of the fact that whatever gastro-intestinal trouble was present was of relatively mild grade, and that toxemia and prostration were due to the pyelitis rather than to gastro-intestinal absorption.

The diagnosis in each instance was made by an examination of the urine. This point cannot be emphasized enough. The

frequency with which febrile disturbances are encountered in the first few weeks after birth makes it absolutely essential that in every case, male or female, pyelitis be excluded. Although most frequently seen in the female sex, these 3 cases show that in the newborn at least pyelitis is just as common in the male as in the female. There are means available by which specimens of urine can be readily obtained from boy and girl babies, and it is essential that in all febrile conditions of the newborn the urine be examined.

As regards the therapy, the alkaline treatment was entirely successful in each instance. As can be seen from the figures, 5 grains of sodium bicarbonate and 5 grains of sodium citrate were given every three hours until the urine was alkaline. Then the dose was gradually reduced, keeping the urine definitely alkaline. Of even greater importance is the necessity of giving large amounts of fluid. The beneficial effects of this were seen particularly in Case I.

To sum up: 1. Pyelitis in the newborn is probably very much more common than we suspect at the present time.

2. The clinical picture shows the same wide variations that it does in later infancy.

3. The alkaline treatment, together with the forcing of fluids, proved successful in these three cases.

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NEPHROPATHIES

THE classification of disease is of much more than academic interest, and serves different purposes. The classification will, therefore, be approached from different viewpoints, and it is often impossible to harmonize the results. This is especially true in the clinical, etiologic, pathologic, and functional classifications of the diseases of the kidney. Bright's disease, in its original significance, is of little more than historic interest, as much more is now included in the name than "a disease of the kidney associated with dropsy and albuminuria."

Until the 90's the structural criteria were the main bases for the classification, and here, as Aschoff says, every pathologist has his own "Glaubens bekenntnis." The correlation of clinical and pathologic findings, using the old terms "parenchymatous" and "interstitial nephritis," has notoriously failed, as has been realized by all clinicians who have followed their cases to autopsy.

In later times much more interest has attached to the study of function, and efforts have been made to correlate the functional with the anatomic findings—Schlayer, Widal, and others. These attempts cannot be said to have been successful so far as concerns the human nephropathies. There has, however, arisen out of these studies a closer association of the clinician, pathologic anatomist, and pathologic physiologist, which has markedly advanced our knowledge of the nephropathies, and evolved a

classification which works better from the standpoint of prognosis, and harmonizes more nearly the clinical and pathologic findings.

The best classification seems to me to be that of Volhard and Fahr, in their monograph, "Die Brightische Nierenkrankheit." Similar classifications have been proposed by Dr. Barker, in Monographic Medicine, Vol. III, 1916, and by Dr. Stengel, in MEDICAL CLINICS OF NORTH AMERICA, September, 1917. Volhard and Fahr's classification is as follows:

A. Degenerative diseases: Nephrosis, genuine and known etiology, with and without amyloid degeneration of the vessels.
   I. Acute course.
   II. Chronic course.
   III. End stage: Nephrotic contracted kidney without increased blood-pressure. Subdivision: Necrotic nephroses.

B. Inflammatory diseases: Nephritides.
   1. Diffuse glomerulonephritis, with obligatory increased blood-pressure. Course in three stages:
      I. The acute stage.
      II. The chronic stage, without kidney insufficiency.
      III. The end stage, with kidney insufficiency.
      } All three stages may run their course: (*a*) without marked edema; (*b*) with marked edema; *i. e.*, with marked and diffuse degeneration of tubular epithelium (mixed form).
   2. Focal nephritis, without raised blood-pressure:
      (*a*) Focal glomerulonephritis:
         I. Acute stage.
         II. Chronic stage.
      (*b*) Septic interstitial focal nephritis.
      (*c*) Embolic focal nephritis.

C. Arteriosclerotic diseases: Scleroses.
   I. The bland, favorable "hypertonie" = pure sclerosis of the kidney vessels.
   II. The combination form: Malignant genuine contracted kidney = sclerosis plus nephritis.

I desire to present a series of cases which we may classify clinically according to this scheme:

CASE I.—S. M., seventeen years of age; male; negro; laborer in a levee camp. *Nephrosis, lues.*

Anamnesis.—Family history negative. Had measles at ten years of age. Pertussis in childhood. Never had scarlet fever or diphtheria. He had "chills and fever" in 1912. He has frequently had sore throat, but does not remember having a severe

attack. Has never had rheumatism. Had an ulcer on penis last year; does not think that it was followed by sore mouth or eruption over the body. Took no treatment for same.

He was admitted to Ward E, Memphis General Hospital, October 31, 1917, complaining of general swelling of his body and shortness of breath. About two weeks before admittance he was much exposed to cold and wet, incident to his work as a laborer in a levee camp. At this time he noticed swelling of his legs and feet, shortness of breath, diarrhea, and general weakness. The swelling gradually increased until it involved the whole body.

Status Præsens.—November 1, 1917: A well-developed negro boy, about seventeen years of age. Mucous membranes of good color. There is a marked generalized edema involving the face, neck, trunk, extremities, and external genitals; signs of fluid in the right pleural cavity; râles over both lungs, front and back.

Heart.—P. M. I. in the fifth interspace, 8 cm. from the mid-sternal line; area of cardiac dulness not enlarged; at apex faint systolic murmur, not transmitted; pulmonic second sound not accentuated.

Abdomen.—Ascites; liver nor spleen palpable. Nervous system negative.

Urine.—Daily quantity not measured, but scant. November 6, 1917: Color, dark brown; sp. gr., 1020; reaction, alkaline; a large quantity of albumin; no sugar; casts present; no red cells or pus cells.

Blood-pressure.—Systolic, 115; diastolic, 70 (auscultatory).

Blood (11/6/17).—Leukocytes, 8000; polymorphonuclears, 58 per cent.; small lymphocytes, 36 per cent.; large mononuclears, 5 per cent.; eosinophils, 1 per cent. 11/12/17: Erythrocytes, 5,182,000; leukocytes, 9000; polymorphonuclears, 66 per cent.; small lymphocytes, 31 per cent.; large mononuclears, 0; eosinophils, 3 per cent. Wassermann reaction positive (++++).

Functional Tests:

MOSENTHAL KIDNEY TEST-DIET, 11/8/17

Time of day	Urine. C.c.	Sp. gr.	NaCl. Per cent.	NaCl. Gm.	N. Per cent.	N. Gm.
8–10	70	1020				
10–12	60	1020				
12– 2	62	1018				
2– 4	72	1020				
4– 6	87	1020				
6– 8	74	1020				
Total day	425	....	.1	.425	1.5	6.37
Night, 8–8	600	1016	.04	.24	1.0	6.00
Total, 24 hours	1025	....	....	.665	....	12.37
Intake fl., NaCl, and N.	1760	....	....	8.5	....	13.4
Difference	+735	....	....	+7.25	....	+1.03

Weight.	Date.	Period.	Blood. Mgm. urea per 100 c.c.	Period	Urine. 24 hrs.	Urea	U. p l.	Ambard
57	11/8/17	4–6	40	87 c.c	1044	18.5	17.7	coeff. .093

R. p. H. (Marriott), 8.2. Phenolsulphonephthalein (intravenously), 2 hrs., 55.

Course.—The patient ran an afebrile course, with pulse from 68 to 86. No discomfort except that attributable to the anasarca and the accumulation of fluid in the serous cavities. There was no evidence of uremia. The anasarca, hydrothorax, and ascites gradually disappeared. After a stay of six weeks in the hospital he left 12/14/17 of his own accord. The urine on his discharge showed sp. gr. 1018; a trace of albumin; hyaline and granular casts. Blood-pressure, S. P. 110; D. P. 65.

Degenerative changes, of the nature of cloudy swellings, occur in the epithelium of the kidney tubules as an accompaniment of most infectious diseases, but there are no clinical manifestations of this other than albuminuria and possibly cylindruria. More severe degenerative changes occur as a result of certain infectious diseases, such as diphtheria, tuberculosis, syphilis, chronic suppurations, viridans sepsis, measles, possibly typhoid and paratyphoid; as the result of endogenous intoxications, as in pregnancy and in malignant tumors; as the result of mineral poisons, as with bichlorid of mercury (nephrosis of known cause). Degenerative changes also occur without discoverable cause (genuine nephrosis).

Clinically these cases show marked general anasarca and transudation into the serous cavities. The fluid is of a pseudochylous nature due to globulin lipoid bodies, is watery and poor in albumin. The urine is of a grayish-yellow or grayish-brown color, cloudy, rich in urates, of high specific gravity, diminished in quantity, exceedingly rich in albumin, and microscopically shows casts, but rarely red blood-cells, and with the polarizing microscope a double refracting substance (Munk).

The functional capacity of the kidney is little impaired, as shown by the various functional kidney tests. There is very little tendency to uremia. The blood is not hydremic, but concentrated, showing an increased number of erythrocytes and increased viscosity. The blood-serum, like the transudates in the serous cavities, is of a pseudochylous appearance. The skin, in contradistinction to the objective blood findings, is often pale, there is frequently anorexia, and a marked tendency to diarrhea. The eye-grounds seldom show any changes, and the general symptoms of discomfort are lacking, except those due to dropsy.

The characteristic features of these cases is the absence of increased blood-pressure and cardiac hypertrophy. In the case presented I desire to call your attention to the presence of lues and the history of exposure to cold and wet as etiologic factors; clinically, to the marked general anasarca, hydrothorax, and ascites—unfortunately the fluid was not examined—to the absence of cardiac hypertrophy; to the large quantity of albumin in the urine and the absence of hematuria; to the blood-pressure, 115–70; to the high blood-count, 5,182,000; to the absence of uremia, and to the results of the functional kidney tests. You will note that there is a high, fixed specific gravity, a slight night polyuria with a fair sp. gr.; a very low salt excretion and a good nitrogen excretion. These results, in the main, agree with the water test, concentration test, and salt and nitrogen excretion in the cases of Volhard and Fahr, which they attribute to presence of the dropsy, due to the increased permeability of the vessels rather than to impaired functional capacity of the kidney. The blood urea is 40 mgm. per 100 c.c. The Ambard 0.093 slightly increased, and the phthalein 55 per cent. in two hours.

The **prognosis** in these cases is not grave, so far as the results of the kidney condition are concerned. Those due to diphtheria and lues frequently run a short course and terminate in recovery. Those due to other causes may run a very prolonged course, even if the edema disappears, the characteristic urine persists and the blood-pressure does not rise, rarely the process in the kidney may pass into the end stage, with contraction and impaired functional capacity, the blood-pressure still not being increased.

If the patient should come to autopsy, according to Volhard and Fahr, in the edema stages, the kidneys will show the following—macroscopically: enlargement, the capsule strips easily, the outer surface is smooth, the substance is more spongy than normal, the cortex is widened and of a smutty appearance, and the medulla is of a brownish color; microscopically: the epithelium, especially of the lower end of the proximal convoluted tubules, shows granular and fatty degeration; that of Henle's loops and the distal convoluted tubules may show similar changes, but not marked, and Henle's loop and the collecting tubules may contain casts. In the malpighian corpuscles there may be fatty changes in the glomerular epithelium. In the capsular space there may be found coagulated albumin and occasionally degenerated epithelium; the glomerular loops are well filled with blood. The interstitial tissue may show slight lymphocytic infiltration and the vessels show no changes unless the nephrosis has developed in a patient with arteriosclerosis.

In the cases which have passed into the stage where the edema has subsided there will be more evidence of inflammatory reaction in the interstitial tissue, and in the end-stage a small contracted kidney, due to marked overgrowth of fibrous connective tissue without evidence of inflammatory reaction in the glomeruli may be found, which may be associated with impaired kidney function, but not associated with raised blood-pressure and cardiac hypertrophy.

CASE II.—Mrs. ———; thirty years of age; housewife; *bichlorid of mercury poisoning—necrotic nephrosis.*

Anamnesis.—Family history negative. No serious diseases in past history. Two children. Domestic infelicity.

At about 8 P. M., May 31, 1916, swallowed 52½ grains bichlorid of mercury—seven 7½-grain tablets dissolved in a glass of water—supposed to have been headache medicine. The patient vomited and complained of pain and burning under the sternum. Her physician was called immediately. He reached the patient in about fifteen minutes. The stomach was washed out thoroughly with milk. Vomiting continued at intervals through the night and mucosanguinolent discharges from the bowels. She voided urine during the night, the last time just before day. Patient was admitted to a private ward of St. Joseph's Hospital, Memphis, about 5 P. M., June 1, 1916.

Status Præsens.—A well-developed, highly cultivated lady, in a good state of nutrition; very weak, but anxious to recover. The mucous membranes of the mouth and throat very red. She complains of soreness of the throat, difficulty in swallowing, burning under the sternum, and griping pains in the abdomen. There were frequent discharges from the bowels—mucus and blood with tenesmus. The temperature was 100⅘° F. and pulse 110.

For nine days there was very great weakness, depression, much nausea and vomiting, frequent bowel movements—six to twenty-seven daily—backache, headache, twitching of the muscles, delirium, hiccup. On June 8th there were very severe hemorrhages from the stomach and bowels. There was severe salivation and stomatitis. There was during this time no edema; later slight puffiness of the face developed.

Urine.—There was complete anuria from June 1st to 9th; on this day about 150 c.c. was passed. It was of a pale, greenish tinge, sp. gr. 1012; faintly acid reaction; a trace of albumin; the centrifuged specimen contained a few red cells, leukocytes, much degenerated epithelium, broad and narrow, finely granular and epithelial casts. The urine rapidly increased in quantity—6/10, 450 c.c.; 6/11, 1190 c.c.; 6/12, 1395 c.c.; 6/13, 1500 c.c.; 6/14, 2580 c.c.; 6/15, 2250 c.c.; 6/16, 1650 c.c., and continued at about that quantity until discharge. On 6/16 phenolsulphonephthalein excretion in two hours 20 per cent.

Blood.—June 3d—three days from onset—the total non-

protein nitrogen was 101 mgm. for 100 c.c.; 6/8, Hb., 30 per cent. (Tallqvist); 6/21, erythrocytes, 1,584,000, Hb., 35 per cent. (Tallqvist); leukocytes, 12,600; polymorphonuclears, 82 per cent.; small lymphocytes, 19 per cent.; large mononuclears, 9 per cent.

Blood-pressure: 6/2, S. P., 135; D. P., 80 (auscultatory).
6/8, S. P., 140; D. P., 80 (auscultatory).
6/10, S. P., 120; D. P., 55 (auscultatory).

The patient was discharged from the hospital 7/7/16. At that time the urine showed: specific gravity 1021; no albumin; no casts. Her recovery has been complete.

In poisoning by mercury we would expect degeneration of the epithelium of the tubules in its purest form, and you might be surprised to note how the clinical manifestations in this case differ from the one previously described, and from what we have said is characteristic for nephrosis. Here we find no marked edema; we note the remarkably prolonged period of anuria; the impaired kidney function; 101 mg. of N. P. N. for 100 c.c. of blood, which later would probably have been much higher, the low phenol-sulphonephthalein output; slight manifestations of uremia, and finally the slightly increased blood-pressure. Differences in the histologic findings will also be encountered. Where in the nephroses cloudy swelling, granular and fatty degeneration were found in the epithelium, especially that lining the proximal convoluted tubules, without marked impairment of kidney function; in the sublimate kidney there is necrosis, cell death, in the same areas with destruction of kidney function. There is no evidence of inflammatory reaction in the glomeruli in either. It has, therefore, been suggested to designate this as necrotizing nephrosis. There is also in the sublimate kidney a tendency to the deposition of calcium in the epithelium, and this, with secondary inflammatory reaction in the connective tissue, is more marked, the more severe and long continued the poisoning. There is also found early marked evidences of regenerative processes in the flat epithelium, pyknotic nuclei, and occasional mitoses. Edema may occur in the bichlorid kidney, but, as a rule, is absent. The frequent presence of anuria is probably

responsible for the slightly increased blood-pressure which occasionally occurs, as well as for the impaired kidney function.

CASE III.—B. W., negro, male, aged thirty-five. Laborer. Clinical diagnosis, acute diffuse glomerulonephritis plus nephrosis (mixed form).

Anamnesis.—Family history negative. Past history negative, except there was a sore on the penis last year, which was not followed by secondary manifestations of lues. About July 1, 1917, he began to complain of pain in the third finger of the right hand. The pain, which was dull and throbbing in character, grew progressively worse. At the end of a week his doctor made an incision in the finger, on the palmar surface. No pus obtained. The condition of the finger grew rapidly worse. Patient says that the bone "rotted and became unjointed." About this time the entire hand and arm became swollen and he had high fever. About three weeks after the first incision was made the finger was amputated. After this there was gradual improvement. Two or three weeks later patient states that he began to have shortness of breath, that his feet, legs, and abdomen began to swell. This has progressively increased, and on this account he was admitted to Ward E, Memphis General Hospital, September 12, 1917.

Status Præsens.—A well-developed negro man, thirty-five years of age. There is marked general edema, including external genitals. The third finger on left hand is absent, amputated at metacarpophalangeal joint. Healing perfect, though the hand is swollen and stiff. Heart apex not located; area of cardiac dulness extends 10 cm. to left of midsternal line. There is a soft systolic murmur at the apex, not transmitted. The pulmonic second sound is slightly accentuated.

Lungs.—Negative, except for the presence of fluid in both pleural cavities, more on the right than the left.

Abdomen.—Ascites—liver nor spleen palpable.

Temperature 97.8° F.; pulse, 64; respiration, 24.

Urine.—9/13: Pale; sp. gr. 1010; alb. heavy; casts; pus-cells.
9/25: Pale; sp. gr. 1010; alb. heavy; hyaline and granular casts; no pus.

Urine.—10/17: Dark straw; sp. gr. 1014; alk. alb. heavy; casts neg.

10/18: Dark straw; sp. gr. 1014; alk. alb. heavy; casts neg.

11/11: Pale; sp. gr. 1010; alk. alb. heavy; casts neg.

Blood.—10/10, Leukocytes, 7400.

11/12, Erythrocytes, 4,200,000; leukocytes, 6400; polys., 63 per cent.; small lymphs., 34 per cent.; large monos., 3 per cent.; eosin., 0.

Wassermann negative.

Blood-pressure: 9/21, systolic, 190.

10/8, systolic, 172; diastolic, 118.

10/16, systolic, 170; diastolic, 115.

11/5, systolic, 145; diastolic, 90.

Functional Tests:

MOSENTHAL KIDNEY TEST-DIET, 11/8/17. DISAPPEARING EDEMA

	Urine.		NaCl.		N.	
Time of day.	C.c.	Sp. gr.	Per cent.	Gm.	Per cent.	Gm.
8–10	280	1010				
10–12	225	1009				
12– 2	215	1011				
2– 4	325	1010				
4– 6	200	1008				
6– 8	250	1012				
Total day	1495	....	.76	11.362	.9	13.45
Night	1244	1008	.8	9.952	.85	10.57
Total	2739			21.314		24.02
Intake fl., NaCl, and N	1760			8.5		13.4
Difference	979			12.79		10.62

Weight.	Date.	Period.	Blood.			Urine.	Urea Per cent.	
Kgms.			Mgm. urea	U. P.	T.	Urea gms.	14	Ambard
65.1	11/8/17	4–6	per 100 c.c.	200	2400	in 24 hrs.		.09
			48			33.6		

Phenolsulphonephthalein, 50 per cent. in two hours.

Co_2 tension alveolar air, 30 (Marriott).

R. p. H., 8.2 (Marriott).

This case illustrates the usual etiology of diffuse glomerulonephritis. It may be said that all nephritides are due to bacteria or their toxins. In the diffuse glomerulonephritis there is usually

a history of streptococcus infection—*e. g.*, scarlet fever, angina, rheumatic fever, erysipelas, or an infected wound. In two or three weeks after the subsidence of the symptoms of the causative infection manifestations of nephritis appear. Usually in focal glomerulonephritis the nephritis comes on coincidently with the infection. Here we have an infected wound—after two or three weeks, symptoms of nephritis.

As said before, clinically increased blood-pressure separates diffuse glomerulonephritis from nephrosis. In focal glomerulonephritis there is also an absence of rise of blood-pressure, but here the presence of hematuria distinguishes these cases from nephrosis. Edema was formerly thought to be one of the distinguishing clinical features of acute nephritis. Many of these cases, however, run their course without ever showing edema at all, and when it is present to a great extent it is, according to Volhard and Fahr, the accompaniment of associated degenerative changes in the epithelium of the uriniferous tubules.

The *blood* usually shows evidence of slight anemia, as in this case (reds, 4,200,000), and especially in cases unassociated with nephrosis, hydremia is present.

The *heart* may or may not be hypertrophied. It is surprising to see how rapidly the heart enlarges in some cases without edema associated with high blood-pressure. Even in a few days there may be observed a heaving, displaced apex-beat, enlargement of area of cardiac dulness, accentuated second sounds at the base, presystolic gallop rhythm, and systolic murmur at apex.

The *urine* usually shows the presence of blood, which gives to it a dark, smoky color. Albumin is present, but usually less in amount than in the nephrosis. The quantity is diminished and in severe cases anuria may be present. The specific gravity is low in the cases without nephrosis, and possibly the lower the specific gravity, the more severe the injury to the glomeruli. The sediment shows red cells, débris, leukocytes, casts, micrococci, and degenerated epithelial cells.

The functional capacity of the kidney is usually not markedly impaired. According to Volhard and Fahr, the water excreted is good, if no edema is present, as is also the salt excretion. The

nitrogen excretion is good. The non-protein nitrogen in the blood may be increased and the ability to concentrate present or absent. Marked impairment of function would seem to indicate the presence of severe extracapillary glomerulonephritis with grave prognosis. In this case the day and night polyuria and the low, rather fixed specific gravity is probably due to the fact that the patient is eliminating edema. The salt and nitrogen excretions are good. The urea in the blood and Ambard's coefficient are within normal limits, as is also the phenolsulphonephthalein output in two hours. There is evidence of slight acidosis in the alveolar Co_2 tension and R. p. H.

General Symptoms.—There is little characteristic in the general symptoms of acute diffuse glomerulonephritis. There may be at the onset lassitude, depression, anorexia, increased thirst, severe vomiting, chills and fever, enlarged spleen; or there may be no symptoms at all. Changes in the eye-grounds are usually absent; nosebleed and hemorrhages into the skin and mucous membranes may be present. The manifestations of uremia may be divided into those associated with kidney insufficiency, such as contracted pupils, dyspeptic symptoms, great depression, weakness, apathy, stupor, urinous odor of the breath, general hypersensitiveness, muscular irritability, muscular tremors, jerking of the tendons, deep breathing, and fall of temperature; and into those without kidney insufficiency, such as convulsions and symptoms which have been designated eclamptic equivalents, such as amaurosis, hemianopia, transitory disturbances in speech and hearing, paralysis, increased reflexes, positive Babinski's sign, stiffness of the neck, Kernig's sign, headache, and vomiting. The uremia with kidney insufficiency rarely occurs in acute diffuse glomerulonephritis, but convulsions are especially liable to occur in children, and they seem to occur independent of the severity of the kidney lesion.

Course.—This is dependent on the severity of the disease, the time at which it is recognized, and the treatment. With early recognition and proper treatment there is marked tendency to recovery, though many cases pass into the second stage of glomerulonephritis—chronic glomerulonephritis—without kidney in-

sufficiency. This patient, who insists on discharge even though he still has an increased blood-pressure and albumin in his urine, is already possibly passing into this stage.

Pathology.—The macroscopic appearance of the kidney in acute diffuse glomerulonephritis shows little that is characteristic, but microscopically the changes in the glomeruli are quite characteristic. Lohlein and Volhard and Fahr lay down as the most important characteristics lengthening and widening of the glomerular loops; absence of blood in the loops and increase of cellular elements in the glomeruli. In the capsular space may be found desquamated epithelium, red cells, coagulated albumin and fibrin; the walls of the capsule may be adherent. In the tubules are coagulated masses composed of red cells, white cells, and coagulated albumin forming casts.

In isolated proximal convoluted tubules may be found granular degeneration of the epithelium, Henle's loops, and the collecting tubules may contain the above-described casts. The extent of the changes in the tubules depend upon the extent of the inflammatory process in the glomeruli to which they belong. Extensive degenerative changes in the tubules are present only in the cases of mixed form—nephritis plus nephrosis.

With severe changes in the glomeruli small-cell infiltration in the connective tissue may be present. There are no changes in the blood-vessels.

CASE IV.—Mr. ———, white, aged forty-two, merchant. Clinical diagnosis, end-stage chronic glomerulonephritis—secondary contracted kidney.

Anamnesis.—Family history negative. He had the ordinary diseases of childhood, but never had scarlet fever or diphtheria. As a youth he had a good deal of sore throat. He has considered himself very healthy until about three months ago, when he began to have shortness of breath, and he consulted me at this time, complaining of shortness of breath, swelling of the feet and ankles, and impaired vision.

Status Præsens.—A well-developed, intelligent gentleman, 6 feet in height; weight 220 pounds and forty-two years of age. The skin and mucous membranes are pale. The feet and legs

are swollen and pit on pressure. He is dyspneic. The lungs are negative except for faint râles at the base posteriorly. The apex-beat is displaced downward and outward; the area of cardiac dulness is increased to the left and right; there is a faint systolic murmur at the apex, transmitted to the axilla; the second sounds at the base are accentuated; orthodiagram 6.5, 11.5, 19.5 cm.; radial pulses equal 90 per minute; pulsus alternans; radials not palpable.

Abdomen.—No ascites, liver palpable two fingerbreadths below the costal margin and tender; spleen not palpable.

Blood-pressure.—S. P., 170; D. P., 100 (auscultatory).

Blood.—Red cells, 2,640,000; Hb., 32 per cent. (Sahli); C. I., 6; leukocytes, 13,000; polys., 84; S. Ls., 8; L. Ms., 8; Eos., 0.

Urine.—Single specimen; pale, sp. gr. 1005; faint trace of albumin; no sugar; casts present; leukocytes and red cells present.

Eye-grounds.—Normal. Impaired vision due to error in refraction. (Dr. Farrington.)

Functional Tests:

MOSENTHAL DIET

	Urine.					
Time of day.	C.c.	Sp. gr.	NaCl. Per cent.	NaCl. Gm.	N. Per cent.	N. Gm.
8–10	200	1005				
10–12	250	1005				
12– 2	250	1005				
2– 4	250	1005				
4– 6	200	1005				
6– 8	160	1005	.45	5.87	.25	4.375
Total day	1310					
Night 8–8	1750	1005	.3	5.25	.288	3.772
Total twenty-four hours	3060			11.12		8.147
Intake fl., NaCl, and N.	1760			8.5		13.
Difference	1300			2.62		5.267

Urea per 100 c.c. of blood, 324 mgm. Phenolsulphonephthalein in two hours, 0.

Under rest in bed, a low protein diet, and measures directed to the heart this patient improved for about two weeks, but within six weeks from the time of examination he died in uremia.

This is a rather typical case of the end-stage of chronic glomerulonephritis—the so-called secondary contracted kidney. Often, as here, we are unable to discover the cause of the condi-

tion. It is, however, always the development of the previous stages. This development may be rapid, requiring only a short time, or extend over a period of years. The previous stages of the disease may be latent so far as symptoms are concerned, and the first manifestations show themselves in the fatal kidney insufficiency associated with cardiac insufficiency, as this case also illustrates. More frequently, however, they run a course of more or less chronic or periodic manifestations.

The increase of blood-pressure in these cases is usually marked and is probably more constant the older the process.

The heart is usually hypertrophied, but, as a rule, not to the same extent as in the scleroses. There is a marked tendency to myocardial insufficiency, as seen in the dyspnea, presystolic gallop rhythm, increase in area of cardiac dulness, swelling of the liver, and edema of the lower extremities.

Edema of the nephritic type is seldom seen unless the nephritic process is associated with marked degenerative changes in the tubules. The urine is pale, different specimens showing a remarkably constant color; increased in amount; albumin is present in small amount, and the sediment shows leukocytes, casts, degenerated epithelium, and detritus.

Renal insufficiency is the chief clinical characteristic of this type of nephropathy. As seen in this case, there is a remarkably low fixed specific gravity, a night associated with a day polyuria, low night specific gravity, low salt and nitrogen concentration, a high urea content in the blood and a low sulphonephthalein output. According to Stengel, Austin, and Jonas there is also in these cases a low plasmachlorid content, as also a reduction in the plasma bicarbonates.

General Symptoms.—There is usually great loss in strength. The patient often presents a cachectic appearance. The skin and mucous membranes are pale, the hair dry, with a tendency to fall out; frequently there are hemorrhages into the skin and mucous membranes, conjunctivæ, epistaxis, menorrhagia. The blood shows a marked tendency to anemia in marked contrast to benign sclerosis.

Changes in the eye-grounds are frequent, hemorrhages as

well as true albuminuric retinitis being present. The most frequent termination is in that type of uremia associated with kidney insufficiency, though convulsions and eclamptic equivalents may occur with cases associated with arteriosclerosis, which is not infrequent.

As said above, the course is variable, but the outcome is always the same—death.

Pathology.—The kidneys in these cases are pale and usually contracted, but the size varies greatly. Microscopically there are the evidences of glomerulonephritis with secondary fibrosis. Due to the repeated injury which the kidneys have sustained, the damage to the glomeruli with atrophy of the tubules belonging to them, and regenerative changes in the remaining portions, there is quite a variegated picture. Very frequently there is an accompanying sclerosis of the blood-vessels.

CASE V.—Mr. ———, white, aged seventy-four. Planter. Clinical diagnosis, benign hypertension.

Anamnesis.—Famly history negative. Has never had any serious illness. Is a large planter and has had much worry. For the past two years has noticed he had shortness of breath on exercise. Lately he has been worried a great deal with cough and bronchitis. Occasionally his ankles swell during the day, but the swelling usually disappears after a night's rest. His doctor tells him that he has a lazy heart.

Status Præsens.—A gentleman in excellent condition of nutrition and does not look as old as he really is. His voice is hoarse and he has a slight cough. His eyes show a distinct arcus senilis; the ankles are slightly edematous. His radials are palpable; the pulses equal and 84 per minute. There is an occasional extrasystole. The area of cardiac dulness is increased to the left. Orthodiagram 4.5, 12.5, 19.5 cm. The heart sounds are clear, the aortic second is accentuated. No murmurs present.

There are râles throughout both lungs. The liver is palpable two fingerbreadths below the costal margin. The spleen is not palpable. The abdomen otherwise negative. Nervous system negative. Temperature, 98⅘° F.

Blood-pressure.—S. P., 195; D. P., 95.

Blood.—Erythrocytes, 5,130,000; Hb., 90 per cent. (Sahli); leukocytes, 8400; polys., 74; Sls., 20 per cent.; L. Ms., 5 per cent.; Eos., 1 per cent.

Functional Tests:

MOSENTHAL'S KIDNEY TEST-MEAL

Time of day.	Urine. C.c.	Sp. gr.	NaCl. Per cent.	NaCl. Gm.	N. Per cent.	N. Gm.
8–10	120	1015				
10–12	155	1013				
12– 2	115	1014				
2– 4	190	1008				
4– 6	200	1006				
6– 8	105	1010				
Total Day	885	....	.7	6.195	.8	7.08
Night 8–8	455	1010	.8	3.64	.9	4.095
Total twenty-four hours	1340	....	....	9.835	....	11.175
Intake	1760	....	....	8.5	....	13.4
Difference	420	....	....	1.335		1.225

Phenolsulphonephthalein in two hours, 50 per cent.

Benign hypertension usually occurs in the advanced periods of life; a hereditary tendency is frequently noted, but the real cause of the condition is unknown.

The blood-pressure is high, and when the disease is well established is constantly so, but in the early stages may show marked variation. The symptoms are more cardiovascular than renal. The heart is markedly hypertrophied, which at first involves the left heart, giving fluoroscopically the so-called sock heart. With relative insufficiency of the heart muscle there is a feeling of oppression in the chest and dyspnea on exercise. Disturbances of sleep are frequent, pounding noises in the ears when the patient lies on the left side, disturbing dreams, nocturnal attacks of dyspnea prevent sleep. The aortic second sound is accentuated, and a presystolic gallop rhythm is frequently present. With greater dilatation signs of decompensation occur. Stasis bronchitis, pulsation in the veins of the neck, systolic murmur at the apex; swelling of the feet and swelling of the liver. Extrasystoles, pulsus alternans, tachycardia, and heart-block may occur.

Edema is lacking in the compensated cases. There are

numerous symptoms on the part of the vascular system—*e. g.*, cerebral hemorrhage—various symptoms on the part of the nervous system due to cerebral vascular changes, Cheyne-Stokes' breathing, etc.

There are few symptoms referred to the renal system. There are only slight changes in the urine except those referred to the failing heart. The functional capacity of the kidneys is little impaired as a rule. The blood count is usually normal. In the eye-ground there is frequently evidence of arteriosclerosis, but never true albuminuric retinitis. Manifestations of true uremia seldom occur.

The course is essentially chronic, and with proper régime the patient's life may be prolonged for an indefinite period. The end usually comes through cardiac insufficiency or vascular accident.

The kidneys may or may not be contracted. There are arteriosclerotic processes in both the large and small vessels, but no evindece of inflammatory changes in the glomeruli.

Case VI.—N. W., male, negro, aged sixty-seven. Laborer. Clinical diagnosis, arteriosclerosis and nephritis—combination form.

Anamnesis.—Family history negative. Had typhoid at thirteen years of age. Pneumonia at about the same time. Smallpox at fifty years of age. Had an arthritis of right ankle then, and of the left five years ago. Had fever and was confined to bed four or five weeks. His present trouble began October 3, 1917, with pain in the right side of the abdomen, shortness of breath, swelling of feet and legs, and hiccup. On account of these symptoms he came to the hospital and was admitted to Ward E, Memphis General Hospital, October 22, 1917.

Status Præsens.—A negro man in rather a poor state of nutrition, mucous membrane pale. He is dyspneic, sitting up to enable him to breathe better, complains of pain in his abdomen, and has hiccup.

Lungs.—Dulness and diminished breath sounds over both bases, râles irregularly distributed over both lungs.

Heart.—Apex located in the sixth interspace, 12 cm. to the

left of the midsternal line; right border of cardiac dulness extends 4 cm. to the right of the midsternal line. Supracardiac area of dulness increased. There is a systolic murmur at the apex, transmitted to the axilla. The aortic second is accentuated and there is a systolic murmur in the area.

Abdomen.—Tender, no rigidity, wall edematous; liver palpable; spleen not palpable.

Extremities.—Feet and legs edematous.

Eye-grounds.—Not examined.

Blood.—Erythrocytes, 4,428,000. Whites, 8400. Polymorphonuclears, 69 per cent.; small lymphocytes, 28 per cent.; large mononuclears, 3 per cent. Wassermann positive (++++).

Blood-pressure.—Systolic, 170; diastolic, 100.

Urine.—Sp. gr. 1015. Albumin; casts.

Functional Tests:

MOSENTHAL DIET, OCTOBER 24, 1917

Time of day.	Urine. C.c.	Sp. gr.	NaCl. Per cent.	NaCl. Gm.	N. Per cent.	N. Gm.
8–10	74	1014				
10–12	115	1010				
12– 2	102	1015				
2– 4	124	1015				
4– 6	200	1010				
6– 8	380	1010				
Total day	995	....	.4	3.988	.18	1.704
Night, 8–8	410	1010	.3	1.23	.32	1.23
Total day, 24 hours	1405	....	....	5.218	....	2.934
Intake fl., NaCl, and N.	1760	....	....	8.5	....	13.4
Difference	353	....	....	3.282	....	9.466

Weight.	Period.	Blood. Mgm. U. Per 100 c.c.	Amt. U. P.	Total	Urine. Qnt. Urea in 24 hours	Urine Per cent. 19.5	Ambard coeff.
65.4	10–12	180	115 c.c.	1380	26.91		.357

Alveolar Co_2 tension, 25 (Marriott); alkali reserve, 7.8 (Marriott); phenolsulphonephthalein 20 per cent. in two hours.

The patient of his own accord left the hospital 11/11/17 improved.

In the combination form there are the symptoms described above plus those due to the associated nephritis, which depend

upon the extent of the nephritic process. The patient begins to lose weight, the skin to assume the characteristic nephritic appearance, albuminuric retinitis is frequent, and symptoms due to kidney insufficiency develop.

The course is variable and death occurs either from myocardial insufficiency, vascular accident, or uremia.

From these selected cases we believe that it is often possible to classify the nephropathies clinically as well as pathologically on a degenerative, inflammatory, and sclerotic basis. But it must be remembered that transition forms and combinations frequently occur which render an exact classification difficult. It, however, has many advantages from a diagnostic, prognostic, and therapeutic standpoint.

CLINIC OF DR. GEORGE S. BEL

CHARITY HOSPITAL, NEW ORLEANS, LA.

A COMPARISON OF THE ESSENTIAL PNEUMONIAS FROM THE STANDPOINT OF THEIR CLINICAL SIGNIFICANCE

ANATOMICALLY, we recognize two forms of inflammation of the lungs, which are determined according to whether the pathologic process has to do primarily with the terminal air-sacs of a lobe or with a bronchus. It is essential in every pneumonia to determine which one of these processes we are dealing with, since it has a direct bearing on the etiology, and thus subsequently on the treatment. It is well recognized nowadays that the type of pneumonia called the lobar or croupous is only caused by some one of the strains of the pneumococcus; while the other form of pneumonia has a variety of exciting agents. In this connection bronchopneumonia is a type of lesion always determined by tuberculous, influenzal, streptococcal, typhoidal, meningococcal, and bubonic infections of the lungs. In my experience the most of these bronchopneumonias are secondary infections of the lungs. In other words, bronchopneumonia usually follows or is superimposed upon some other infection. With the exception of the pneumococcal infection of the pulmonic tissue the injury invariably begins in connection with the terminal bronchial twigs. The pneumococcal infection, on the other hand, never shows the focus of injury in the bronchial tree. Furthermore, no injury whatsoever can be demonstrated, though it is thought that possibly the lining epithelial cells of the air-sacs are injured in this form of pneumonia.

Lobar pneumonia which is produced by one of the several variants of a pneumococcus species invariably has a sudden abrupt onset, with more or less fever, chill, pain, and symptoms

of toxemia. The lung is found to have involved at least a lobe. In other words, there is a large focus of infection, which is in marked contrast to a small focus or foci, so characteristic of the other form of pneumonia. A physical examination early in this infection reveals that a large portion of the lung is involved, which is never the case in the early part of the broncho type of the infection. Of course, it must be recognized that bronchopneumonia that is rapidly advancing and has been under way for some time may give you the same amount of lung involvment as seen in lobar pneumonia. It is this very point that I wish to stress, since I believe that too often a bronchopneumonia is mistaken by the clinician by the physical signs for the lobar type. This is especially true of the so-called deep-seated central lobar pneumonias, which, in reality, are broncho in type, borne out by careful and painstaking autopsy study. Furthermore, it is a matter of clinical as well as pathologic knowledge that lobar pneumonia is a simultaneous involvement of a whole lobe or lobes, while in bronchopneumonia this is never the case. On the contrary, the bronchopneumonia begins insiduously as a deep-seated bronchitis with subsequently the slow development of small contiguous areas of consolidation. There may be and there often are multiple foci of infection in bronchopneumonia, which in part account for the patchy nature of the consolidation, while in lobar pneumonia there is always one large focus.

As to the inflammation, there is no essential difference in the exudate of either pneumonia. They are both acute, and may be characterized by serous, purulent, or fibrinous accumulations. There is this difference, however, that in the one, namely, lobar, the exudate is confined to the terminals of the respiratory tree, it having begun and ended here; in bronchopneumonia the exudate is not only in the terminal air-sacs of one or more systems, but it is in the interstitial tissues, such as the peribronchial and interalveolar structures, and in every instance begins in the lining of the bronchial tree. The areas of consolidation are secondary to the primary bronchitis, having developed subsequently as an extension from the original focus. In this fact we have an explanation of the development from time to time in

the course of bronchopneumonia of new isolated foci of consolidation. In other words, a new crop of lesions may appear from time to time during the course of infection. These new foci are always at first small and scarcely to be detected, but if carefully followed will be found to gradually increase in size. As time goes on these bronchopneumonic foci may attain such a size as to meet or coalesce, giving us practically a whole lobe involvement. If the case is seen at this period of the disease it is readily understood how the clinician may wrongly call it one of lobar infection. However, if you bear in mind what I just said you may avoid confusing the bronchopneumonia with the lobar pneumonia; as in the former, even though the whole lobe is practically solid, you will detect on careful physical examination a variety of signs indicating that the inflammatory process is of various stages, though we do not recognize in bronchopneumonia the gross pathologic stages of lobar pneumonia, such as engorgement, red and gray hepatization.

I wish to emphasize that it is well to remember in uncomplicated lobar pneumonia the lung tissue in convalescence is returning to normal; while in bronchopneumonia the lung, at best, is only partially normalized. This is because in the one the inflammatory process did not involve the supporting tissue of the lungs, and in consequence resolves without organization; while in the broncho type the inflammatory process involves the supporting tissues and, of necessity, is organized during repair. To state in other words, recovery after lobar pneumonia leaves the lung, in an uncomplicated case, anatomically and physiologically as it was before the infection; in bronchopneumonia the lung is in these respects invariably impaired. The importance of this is obvious. For example, a lung thus permanently impaired, even though slightly, renders it vulnerable to other infections, more especially tuberculosis. In children this is particularly the case where pulmonary tuberculosis develops subsequently into a bronchopneumonia.

Now gentlemen, I shall bring before you cases which illustrate what I have had to say about the essential pneumonias. We will now study and discuss together these cases by carefully comparing

the clinical symptoms and physical signs so we can intelligently interpret the pathologic processes which underlie these essential pneumonias.

This case, negro male, age thirty-one; occupation laborer, admitted to my service March 15, 1918; previous history unimportant, as it has no bearing on his present illness.

Present Illness.—Patient taken suddenly sick four days ago, while at work, with classical symptoms of lobar pneumonia.

At this bedside examination we notice the following symptoms and signs: Temperature 104⅘° F., which has oscillated between 103° and 104⅘° F. since his admission. Pulse 130, varying between 118 and 124, of fair volume and regular. Respiration 44, slight delirium, herpes on lips, and, as you notice, the patient grunts on expiration. This individual is coughing and expectorating sputum which is tenacious and blood stained. Blood-picture in this case shows a leukocytosis of 26,000; the culture reveals the pneumococcus, which not only agglutinates with the patient's blood, but with a monovalent serum, classifying it as strain No. 3. Blood-pressure at this time is 118 systolic. The urine, as you notice, is one of any acute infectious disease.

The following physical signs are present:

Respiratory movements and expansion are much diminished on the right side; tactile fremitus is greatly increased and absolute dulness over the whole right lower lobe and marked bronchial breathing, with bronchophony.

The second case is one of bronchopneumonia, of influenzal etiology. This case, a negro male, aged eighteen, occupation laborer, admitted to my service on March 10, 1918, with a history of having a severe coryza, cough, slight fever, and indefinite pains over various parts of the body. As in the other case, the patient's past history is of no moment.

Now, gentlemen, what are the clinical symptoms and physical signs to be found in this case? We will determine these and then compare them with those of the lobar case.

Let me call your attention to the fact that the onset of the lung infection was secondary to the infection already existing in the upper respiratory tract and that it began insidiously, develop-

ing gradually without a chill or high fever and very little additional signs and symptoms to those present prior to the lung involvement, which is in contrast to our other case there of lobar pneumonia. We have said that this bronchopneumonia is influenzal. The statement is made on the laboratory findings of Pfeiffer's bacillus in large numbers in the sputum. The agglutination reaction of the patient's blood is also positive. While we know the influenza bacillus is responsible for the bronchopneumonia, it may not be entirely so. We must bear in mind that this and other bronchopneumonias have two or more causal agents working conjointly. We call this case influenzal bronchopneumonia because there are laboratory reasons pointing to the fact that the Pfeiffer organism is playing the most important rôle.

At this examination we notice the following symptoms: His temperature is 103° F. and is of an irregular type, in that, as we see by the chart, there is a range of 3 degrees within a twenty-four-hour period, which was not like that in our chart of the lobar patient. The cough is persistent, frequent, and of a dry character, also differing in this respect from the cough of the lobar patient. It is a significant fact that in this patient there is no acute pain in the chest like we have in our other case, which indicates the inflammatory process does not involve the pleura so typical of the lobar type. This patient has dyspnea and rapid pulse that does not differ from the other pneumonia, and the explanation is the same. The blood-picture in this case is interesting. While we have a leukocytosis, it is slight compared with the one we have in the other patient. The increased neutrophils are due to the mixed infection, because pure influenzal infection would give us a leukopenia. Therefore the leukocytosis here is further proof that the bronchopneumonia is caused by two or more etiologic factors.

The chief physical signs are indicative of isolated areas of consolidation intimately associated with bronchitis. While we cannot detect here from this single examination that the solidifications are increasing in size and new ones developing, we can tell you, however, that such is the case. Day before yesterday I

noticed that several of these pneumonic patches found today were much smaller and that we have others that were not present before.

To appreciate the pathology of bronchopneumonia one must go over the physical signs from day to day, for in no other way can you perceive that the inflammation is spreading insidiously by continuity and contiguity. All of this is in marked contrast to the development of the process of our lobar pneumonia case. We notice scattered areas of impaired resonance, with alternating hyperresonance, also detect subcrepitant râles occasionally, but the predominating râle is the pipling dry type which outsounds the other in loudness. This kaleidoscopic change is only appreciated by an understanding of the pathology. Just as we have changes from day to day in the size of the consolidation, so have we changes in the consistence of these areas which explains why an area resonant yesterday may be dull today and why these râles also vary in position and in character. The loud wheezing râles in bronchopneumonia are due to the inflammation of the bronchioles, which is a primary and continuous process of this disease.

Now gentlemen, to explain these symptoms and signs we must bear in mind the anatomy, physiology, and pathology of the organs involved. While we here are concerned mainly with the pathology, we cannot understand this unless we know the anatomy and physiology; the three are essential if you are to appreciate the signs and symptoms in this case. Students of medicine must have an explanation of the various manifestations on the part of the host who is combating an injurious agent if they are to intelligently diagnose and subsequently treat the disease. Too often the student learns a group of signs and symptoms for a given infection without understanding their mechanism of production, and for this reason I will now proceed to elucidate the symptom-complex that we have here before us occasioned by the pneumococcus infection of the lungs.

The temperature is occasioned by what? In a general way we say that all infectious diseases give us increased body heat, which is true; but does not explain its mechanism of production.

We believe it is the result of the direct action upon the body cells by the poison elaborated by the pneumococcus. This action of the poison upon the cells increases their activity and thereby causes more heat production. There is also a direct stimulation by the poison upon the heat-producing centers which is not commensurate with heat dissipation. We said the pulse-rate or heart action and respiration are increased in this case. Why? The explanation of the cause is rather complex. Three factors at least are concerned. In general, we may say the specific poison is directly or indirectly responsible. The poison produces pyrexia in the manner previously mentioned, and this fever accelerates the heart because of the increased body heat. Second, the poison is thought to have a depressing effect upon the inhibitory cardiac fibers of the vagus, which permits, in consequence, an acceleration of the heart action. Third, and I think most important, is the direct action upon the parenchyma of the heart by the poison which brings about weakening of the heart muscle because of the degeneration. This lowers the blood-pressure; and the heart, to compensate, beats faster. Furthermore, the lowering of the blood-pressure means less oxygenation. There is one thing I wish to call your special attention to, and that is, that the consolidation of the lung is in no way responsible for the increased heart action, the dilatation of the right chambers, or the dyspnea. If the solid lung was the cause of these symptoms, how do we explain the rapid return to normal of the heart, its action, and the dyspnea immediately following the crisis, when we know that there are several days during the resolution stage in which the lung is still solid, as demonstrated upon physical examination? The *herpes* is thought to be the result of irritation and stimulation of some one of the posterior root ganglia. The *pain* which is so common and constant with lobar pneumonia is due to the inflammatory process involving the pleura. The pain is the expression of irritation of the nerve-endings by the toxin, more so, we think, than we formerly thought, to the pressure or stretching of the nerve-endings by the surrounding exudate. In this connection let me impress you with the fact that lobar pneumonia is always associated with pleurisy, differing in

this respect from the broncho type; except in those cases, and as a rule, few in number, where the inflammatory process begins at the periphery or extends to the periphery. It may be said that no bronchopneumonia begins with an acute pleurisy, because even with those cases where the focus began at the outer margin the inflammation was not exactly in the pleural surface, but some distance below. Regarding the sputum in the early stage, it is likely to be scant and of a mucoid nature. Later it becomes more profuse, blood streaked, or rusty colored. In bronchopneumonia there is always more expectoration in the disease and its character is mucopurulent, and not so likely to be blood stained, and rarely rusty. This difference in the sputa in the two pneumonias is readily explained by the pathology. In lobar pneumonia the sputum is composed largely of the hypersecretion from the respiratory tubes; while in bronchopneumonia it is the actual inflammatory exudate mixed with the hypersecretion. The sputum in lobar pneumonia is thick and tenacious because of the mucus predomination, and later on in the disease when it becomes creamy it loses its tenacity because of the preponderance of inflammatory exudate which has undergone more or less digestion. The rusty color of the sputum is due to the blood which has hemolized. The blood-picture in lobar pneumonia does not differ materially from bronchopneumonia or, for that matter, from that of any other pyogenic infection. It is the rule to have a very high neutrophilic leukocytosis in lobar pneumonia for the reason that there is a tremendous focus of acute inflammation which drains a large vascular area of the essential cells of acute inflammation. Without exception lobar pneumonia is the largest acute inflammatory area that we know for any infection. In explanation of the occurrence of leukocytosis we believe that it is the replenishing of the normal neutrophilic element to the circulation by the blood-making tissue in lieu of the loss occasioned by the tissues inflamed. The local attraction or positive chemiotaxis of the leukocyte is enormous in lobar pneumonia because of the size of the lung area involved, together with the fact that there is a large number of blood-vessels that are normally present of necessity in the lung. The drain on the vascular system

through the vessels involved is so large there must be a compensatory replenishment of the neutrophils to the circulation. It might be asked, Why the need on the part of the host for an increase above the normal leukocyte in the circulation during lobar pneumonia infection? I believe there is no need, but in accordance with Weigert's law of superproduction we have the true explanation of the circulatory leukocytosis. The blood-making tissues are called upon to make up the loss in neutrophils which have been attracted from the vessels to the inflammatory focus; and in making up the loss the tissues overdo it, just as we have in the case of repair to an injury or the production of antibodies. It is well to remember occasionally we may have in lobar pneumonia a low leukocytosis or even a leukopenia, which signifies in both instances a low-grade resistance on the part of the patient and necessarily a poor prognosis.

In explanation of certain physical signs presented in this case I wish to say they are, in general, brought about by the nonfunctionating solid lung tissue. The lagging or immobility of the affected side is the result of pain from the pleuritis and the consolidative pulmonic tissue. The other physical signs, such as increased tactile fremitus, dulness, bronchial breathing, and bronchophony, are due to the solidification of the lung tissue. The consolidation is due to the obliteration of the normal air spaces by exudate, which has eliminated the air. The exudate is derived almost entirely from the interalveolar capillaries, with the exception of the fibrin and desquamated epithelial cells of the air-sacs. The fibrin, one of the main constituents of the exudate, does not appear early in the pneumonia because it is derived later from the elements of the exudate which has already arrived. Fibrin, unlike the neutrophils, serum, and red blood-cells, is subsequently formed in the air-sac spaces, the result of fibrinogen and lime salts of the serum and nucleoprotein or ferment from the disintegrated neutrophils. The greatest degree of solidity in lobar pneumonia is when the maximum of fibrin has been obtained. The lung at this period is not only solid but granular, gray, and dry. The degrees of consolidation are explained by the character of the exudate. Early in the disease the exudate is

chiefly serous and does not take up the entire air spaces, which gives you a less firm consistence, together with considerable sponginess because of the contained air not yet excluded; later in the disease the exudate becomes less fluid and more solid because of the appearance now of more cells and fibrin and the complete exclusion of air. It must be remembered that after the crisis the lung again approaches the original consistence by passing from the greatest degree of firm solidity to a semifluid and then a fluid, and finally an air-containing fluid consistency, indicating that the air is again returning.

While I have not attempted to describe the entire symptom-complex of this case of lobar pneumonia, I have taken up what I think are the essentials.

Lobar pneumonia terminates in resolution with a complete return of the lungs to normal, or in partial resolution with more or less organization, resulting in permanent impairment or fibrosis of the lung after recovery. Complete resolution is the more common of the two favorable endings, and is, of course, to be desired. It is of interest to know that in uncomplicated pneumonia with recovery we have the only example of an extensive inflammatory exudate being removed without organization. The termination in the ordinary case in this infection is what we commonly term "crisis," that is, a sudden sharp fall in temperature to normal. The cause of the crisis is the neutralization of the pneumococcal toxin by the antisubstances that have now been developed by the host in sufficient quantity. Pneumonia when uncomplicated is a self-limited disease with a sudden onset, profound toxemia, and abrupt termination, after a serious illness of about from seven to nine days.

The **treatment of lobar pneumonia,** aside from supporting, should be serum therapy. Regarding the treatment other than serum the principal object is to support the patient in every way possible, to augment his powers to resist the inroads of the infection. In other words, to meet the indications as they arise, bearing in mind that drugs have no specific action and are to be avoided as much as possible. It hardly seems necessary for me to mention that fresh air, nutritious diet and stimulation, when

indicated, should be administered. It is essential in this connection to determine as early as possible the type of pneumococcus giving rise to the pneumonia. I do not advocate determining the type from the sputum or upper respiratory tract when we have a much shorter and more satisfactory route. All pneumococcal pneumonias are septicemias; particularly is this true in the early stages of the disease. To work out the strain from the sputum means first a separation from the upper respiratory flora, as well as the separation possibly from other strains of the pneumococcus. This is time-consuming, whether you use the cultural or animal method of differentiation. On the other hand, a culture from the blood gives you the organism pure, which can be immediately tested against the various immune sera to determine the type. Even in the event of failure to recover the organism from the blood-stream, stock pneumococci, representing the four strains, can be tested against the patient's blood, which in my experience contains sufficient agglutinins as early as the second day of the disease to diagnose the type of the infection. Three days at least are required to determine the pneumococcus strain when the sputum is employed. As to the value of the various types of pneumococcal antitoxins, we infer from Cole, of the Rockefeller Institute, that the serum for type 1 is highly efficacious, while for 2, 3, and 4 its value is questionable.

While speaking of specific treatment I would like to state that vaccine therapy, whether the plain or sensitized product is administered, has not in the experience of most clinicians yielded results. In my opinion, vaccines for the cure of pneumococcal pneumonia has failed completely. I strongly advise the serum therapy for lobar pneumonia because it undoubtedly is beneficial in certain types of the infection and may be of considerable value in other types. Unlike vaccine therapy, serum cannot be harmful in any case. There is always the question of overburdening the immunity mechanism by the introduction of more poison, which one is invariably doing when he injects specific vaccines. Vaccines, I believe, we may say unreservedly are more likely to be beneficial in localized than in generalized infections. Lobar pneumonia, in the strict sense, is not a localized infection, for, as

I have indicated to you from the beginning of this lecture, the disease is a bacteriemia, producing changes toxic and otherwise in various parts of the body than the lung.

We hope and we have good reason to believe from the advance in serum therapy made by Dr. Cole that the time is not far distant when we will have a specific treatment for lobar pneumonia as efficacious as we have for diphtheria.

The **treatment of bronchopneumonia** is based largely upon the determination of the injurious agent, that is, as far as specific treatment is concerned, and in the experience of all, this is decidedly limited in its effect. Theoretically, vaccine or serum therapy is advocated, but practically it has not yielded results. So many of the bronchopneumonias are secondary infections and localized, that vaccines suggest themselves for treatment. As a preventive measure against the development of this type of pneumonia vaccines might be advocated, for example, influenzal infection primarily in the upper respiratory tract if administered at this time may prevent the subsequent development of bronchopneumonia. As far as non-specific treatment is concerned, what has already been said about the lobar type applies to the bronchopneumonia.

TYPHOID FEVER COMPLICATED WITH PURULENT CEREBROSPINAL TYPHOIDAL MENINGITIS AND NO INTESTINAL LESIONS

THE case which we have for conference today is one which has been under our observation in the ward as typhoid fever with meningitis. The object of this conference is to establish from the postmortem findings to what extent we were correct in our clinical diagnosis. This case is one of unusual interest because of the cerebrospinal inflammation, which has been prominent since three days after his admission to the ward seven days ago. Shortly after admission the meningeal symptoms became so marked in this case of typhoid fever we suspected metastasis to the brain or a superimposed infection due to some other microorganism. To clear up this point a lumbar puncture was made and a very turbid fluid removed, which, on microscopic examination, revealed the Bacillus typhosus. Prior to the meningeal involvement the case presented many of the clinical features of typhoid fever, which was confirmed by the laboratory through a positive blood-culture and a positive Widal reaction.

Purulent meningitis due to the Bacillus typhosus is exceedingly rare as a primary infection, and not at all common as a complication in typhoid fever. I do not wish you to confuse actual infection of the meninges by the typhoid bacillus with the clinical meningismus, which is not at all uncommon in typhoid patients.

Now, gentlemen, before we begin the autopsy, we will review the bedside findings together with the history of the case.

J. K., white, male, aged twenty years, occupation laborer, native of Louisiana, admitted to my service in the Charity Hospital April 2, 1918.

Previous History.—Had the usual diseases of childhood, otherwise unimportant.

Present Illness.—About eight days ago began to complain of slight frontal headache, general malaise, and on one occasion had a slight chill. On admission he presented the following symptoms and signs: Headache, fever (102⅖° F.), pulse 96, respiration 26, tongue coated with red edges. Lungs and heart were negative. Abdomen was distended and sensitive. Spleen and liver palpable. There were no rose-colored spots to be detected, white blood-cells 7000, with 64 neutrophils, 36 lymphocytes. Widal positive. At this time a blood-culture was requested and forty-eight hours later reported upon as positive to typhoid fever.

The signs of meningeal disease appeared three days after admission and a lumbar puncture was made at once. The spinal fluid was under pressure and turbid. A pure culture of the typhoid bacillus was recovered. From this date the patient presented the classical symptoms of meningitis, such as rigidity of neck, divergent strabismus, absence of patella reflex, and positive Kernig. Twenty-four hours before death patient became convulsive and comatose.

I shall not take up too much time with the explanation and description of the symptomatology that was presented in this case because we are anxious to see the pathology. After the postmortem, which is to be held immediately by my colleague, Professor Duval, we will together discuss this case from the pathologic and clinical aspects. I wish to impress the class with the importance of postmortem study of all cases, and particularly cases that have been followed by the students in the wards. There is no better way of learning your medicine than in conference at the autopsy table.

Postmortem Examination.—*Summary of the Protocol.*—The body is that of a well-developed and nourished white male, length 160 cm. Rigor mortis is marked; lividity is noted in the depending parts of the body. There is no edema. The pupils are equal and measure 4 mm.

Peritoneal cavity contains about 100 c.c. of a reddish-colored fluid. The omentum is short and curled up about the transverse colon. The mesenteric lymph-nodes are enlarged throughout and

on section are distinctly meaty. The appendix is negative and measures 15 cm. in length. The diaphragm reaches the fifth interspace on the left and fifth rib on the right.

Pleural cavities contain a slight excess of clear fluid, otherwise negative.

Pericardial cavity is negative.

Heart weighs 330 grams, but otherwise normal, except that it is somewhat friable. The endocardium and valves are negative.

Lungs are negative.

Spleen weighs 290 grams, is enlarged, and rather soft. The malpighian bodies are obscured. The splenic pulp is very soft, chocolate brown in color, and readily comes away on scraping.

Liver weighs 2020 grams. On section, the cut surface presents many yellowish areas, ranging in size from a dime to a silver dollar. The gall-bladder and ducts are patent.

Pancreas is negative.

Gastro-intestinal tract is absolutely negative throughout. In other words, there is no evidence of ulceration of any description. Peyer's patches and solitary follicles are normal.

Adrenals are normal.

Kidneys weigh 650 grams. The capsule is tense and, on section, the cut surface presents a swollen, cloudy appearance. The malpighian tufts are enlarged and distinct as elevated tiny red dots. The cortex measures 8 mm. in greatest depth.

The organs of the neck are negative.

Genital organs are negative.

Head covered with short, light brown hair. Scalp and calvarium are normal. Dura non-adherent. Villi numerous. Brain weighs 1400 grams. On opening the dura the pia and arachnoid are markedly injected, and there can be noticed beneath that the brain is bathed in a purulent exudate. The convolutions are flattened and the sulci are correspondingly obliterated. This exudate is found most marked over the cortex, though it is present everywhere beneath the covering of the brain and spinal cord. On section of the brain, the ventricles contain a slight excess of fluid which is turbid. The nasal ganglia, pons, and medulla show nothing remarkable.

Cultures from the heart's blood and exudate of the meninges subsequently revealed a pure growth of Bacillus typhosus.

Anatomic Diagnosis.—Typhoid fever, without intestinal lesions; typhoid cerebrospinal meningitis; typhoid septicemia.

From the anatomic findings we notice that the gross lesions in the spleen, the liver, the lymph-nodes, and the kidneys are those of classical typhoid fever, which bears out our clinical diagnosis in this case. The most interesting features of the autopsy are the absence of typhoid lesions in the intestinal tract, and the presence of purulent typhoid cerebrospinal meningitis. Both are unusual. To explain the absence of any intestinal lesion we might say that the case, because of the meningitis, died before they could develop; or, on the other hand, that the intestinal lesions, because of the long duration of the disease, had healed. Against the first hypothesis is the normal condition of Peyer's patches and solitary follicles. Cases of typhoid dying from toxemia in the intestinal pre-ulcerative stage always show a more or less swollen condition of Peyer's patches. Even where it is too slight to be detected in the gross, there is abundant microscopic evidence which is unmistakable. On the other hand, the intestinal lesions, had they existed, and had healed, would show evidence in the Peyer's patches of either scarring or pin-point areas of altered hemorrhage. We can assume from the facts in hand that no intestinal lesions of typhoid existed in this case.

Turning to the meningitis, we are not only struck with its extent, but with the character of the inflammatory exudate. The typhoid bacillus is ordinarily not a pus producer, but excites a proliferative reaction on the part of the host. When, however, it plays the rôle of a pyogen it is extremely interesting because unusual. In this case we have positive evidence of the organism playing a twofold rôle, namely, exciting proliferation in one place and exudation in another. This condition is so unusual for the typhoid organism that we are obliged to look with suspicion upon the purulent exudate as of typhoidal origin until all other organisms are bacteriologically exhausted, which has been done in this instance.

It used to be held by some good authorities that typhoid

primarily is always an intestinal infection. We see in this case that we have another exception to the rule. This case also demonstrates the importance of recognizing the possibility of typhoid meningitis either primarily or secondarily.

It is of interest to know whether the infection began in the meninges or in the circulation. We conclude from the history and clinical symptom-complex that it began in the circulation as a septicemia. It is my belief that all cases of typhoid, whether primarily meningeal or intestinal, arise as metastatic lesions from the circulation. A fact ever to be borne in mind in the ordinary classical case of typhoid fever is that there is a bacteremia at the time of the appearance of the earliest symptoms, indicating that the blood lesion existed even before or, we might say, in the presymptom stage of the disease.

We have seen here the enlarged spleen, mesentery lymph-nodes, and liver. Does it occur to you what has occasioned this increase in size of these organs? The pathologist teaches us that it is due to an excessive accumulation of endothelial phagocytes, and not to an ordinary hyperplasia.

CLINIC OF DR. CHARLES L. MINOR

ASHEVILLE, NORTH CAROLINA

ARTIFICIAL PNEUMOTHORAX (FORLANINI). ITS APPLICATION TO THE ARREST OR CURE OF PULMONARY TUBERCULOSIS

Complete Description of Technic. Complications and How to Meet Them. Management of Cases

THE patient I wish to present to you today is a case of bilateral pulmonary tuberculosis whom I have watched for some months, hoping that I could rally his resisting powers so that he might be enabled to arrest the disease which has been slowly but steadily advancing in his left lung. While some authorities have advocated using artificial pneumothorax in incipient cases of pulmonary tuberculosis, I have never felt that this was wise. Rational treatment applied in such cases gets such a high percentage of good results that I do not think we are justified in using such a serious procedure as the total putting out of commission of a slightly involved lung, especially when we cannot promise the patient that this lung will finally re-expand and be as good as ever—a thing which occurs in some cases, but by no means all. It is in obstinately advancing or advanced cases like the one I present to you that I think we have full justification for applying this procedure. The process, as I have said, is slowly but steadily advancing despite all treatment. There is marked evidence of toxemia with all its baneful effects upon the patient's constitution and resisting power, and yet the amount of trouble in the better lung is so mild that we can feel reasonably sure that it will safely take up the burden of the double work thrown upon it if collapse is not carried on too rapidly. It would seem certain that without some other help this case will go steadily down hill, whereas, by

using compression, we can offer him, I believe, a fair prospect of arresting this advance and a great probability of stopping the disastrous toxemia which is killing him, unless adhesions prevent complete collapse or some complication causes us to fail. Moreover, it may enable us to scar down the trouble in the lung and to return him to working efficiency. Statistics have shown that applied to moderately advanced or advanced cases, many of which might reasonably be called utterly hopeless, we can expect from 10 to 20 per cent. of satisfactory results, and with care in its application need have no great fear of any mortality from the procedure.

The case I present is Mr. A. C. D., age thirty-two; single; occupation bank-clerk; home, New York City. His family history is absolutely negative to tuberculosis, "chronic bronchitis," anemia, neurasthenia, or dyspepsia. His childhood history from the first to the seventh year is negative. From the seventh to the eighteenth year the patient attended day school, and while he had numerous winter colds and tended to be rather thin, he, during this time, had no severe sicknesses and passed as a well boy. At eighteen he took up clerical work and has had various bookkeeping positions since, his work places having been usually ill ventilated and dark. I might here note that the conditions under which our bank and other clerks habitually work are too generally unpardonably unhygienic. Spitting on the floors is not prevented, spittoons are often absent or not used, air and sunlight are at a premium, the hours are long, and in rush seasons overtime is the rule without any extra pay for it. That the incidence of tuberculosis under these conditions is heavy is not to be wondered at. Some of our larger and more modern banks have most excellent conditions, but the majority of our small banks both in cities and small towns, and of our offices, should be investigated by our Boards of Health.

Entering on his present job at twenty-four, he worked from 8 A. M. until 6 P. M., but in rush seasons overtime was often demanded until as late as 11 or 12 P. M. Three spittoons were all that were at the service of the whole office force and spitting on the floor was necessarily common, several of the clerks having

chronic coughs and expectoration. His home conditions were fair and the food good, but he usually had to rush his morning and midday meals. His average weight has been 140 pounds, the best in his life 157 pounds, his insurance standard weight should be 165 pounds. He denies alcoholic dissipation and lues. He admits an occasional moderate use of alcohol. Sundays were spent in rest and recreation. From eighteen to thirty-two, barring the present sickness, he has had no severe illness, but has continued to have winter colds. The patient says he was in his usual health until the age of thirty, when his work began to tire him unduly, and he would wake up tired in the mornings and wear out by mid-afternoon. That winter he had a worse cold than usual and the cough became chronic and was accompanied by a little mucopurulent expectoration, which disappeared that summer. Although he was losing weight he paid no attention to his symptoms until the autumn, when one day, without cause, he suddenly brought up about ½ ounce of bright blood. The family doctor told him, without physical examination, that this was due to the breaking of a vessel in the back of his throat, so he did nothing for it, but when this occurred again shortly before Christmas he went to the clinic, where a careful examination showed an active process of the upper third of his left lung. When I first saw the patient he was a somewhat emaciated man, with unduly bright eyes, a slight flush in the left cheek, a moderate amount of supraclavicular flattening, a marked left shoulder droop, and considerable limitation of the motion of the shoulder on breathing. The chest was fairly built, though a little too long and rather flat. The patient is left-handed, yet the tape shows the left side markedly smaller than the right, and the expansion of the left side 1 inch less than the right. The larynx is negative. There is considerable pyorrhea, with poor teeth, and there is marked obstruction of the right nostril by a spur. Percussion shows the isthmus of the left apex to be narrowed, being only 1¼ inches on the left, 2 inches on the right. The motion of the base of the left lung between rest and extreme inspiration is 1 inch; of the right, 2 inches. There is dulness L. U. A. to the third rib and a shortened percussion note to the fifth. There is

also dulness L. U. P. to the spine of the scapula, impaired resonance to the angle of the scapula. In the right supraclavicular and supraspinous fossæ there is slightly impaired resonance. Over the upper left lung behind there is bronchial breathing to the second rib, with bronchovesicular breathing to the fourth rib and rather feeble breathing to the base. Over the upper left lung in front to the third rib there are medium and fine moist râles, commonly but unfortunately called "subcrepitant râles," and from this point down to the fifth rib patches of crepitations. Posteriorly on the left the moisture extends to the spine of the scapula, below which there are fine dry crackles to the angle, with bronchovesicular breathing from apex to midscapula. Over the right clavicle there is feeble breathing with one or two very fine dry inspiratory crackles on cough. The patient reports a loose, increasingly productive cough on and off all day, with about 1½ ounces of mucopurulent expectoration, chiefly on waking, at which time it is heavier and green. The temperature, which is subnormal in the morning, reaches 101+° F. by 4 P. M., despite rest, falling slowly, until by 10 o'clock it is normal. There are no chills, an occasional sweat, the pulse varies from 80 to 110. There is moderate anorexia, with considerable fermentative dyspepsia. There is considerable dyspnea on exertion, but none while at rest. There is no hoarseness or dysphagia. The weight today is 115 pounds. While he has made small symptomatic gains during the four months he has been under treatment, the process on the left has extended steadily and the *x*-ray shadow has shown advance, there being today with the fluoroscope dense shading in the upper left to the third, with cloudlike mottling below extending nearly to the base. The right apex is not entirely clear, and there is considerable thickening of the peribronchial glands shadow connected on the right with the apical shadow. There are, fortunately, no evidences of pleuritic adhesions in the left lung. The motion of the left base, while limited, is not abrogated, and none of the other measures of examination justify a belief in such adhesions. As I interpret it, we have here an advancing tuberculous bronchopneumonia in the left lung, with beginning softening of the upper

lobe, and a slight catarrh of the right apex. We have given rest, feeding, air, and the usual hygienic and medical procedures a fair trial, and they have been entirely ineffectual, and while no case is so bad that it may not possibly become arrested, there is no reason in this case to anticipate such a thing. I have no

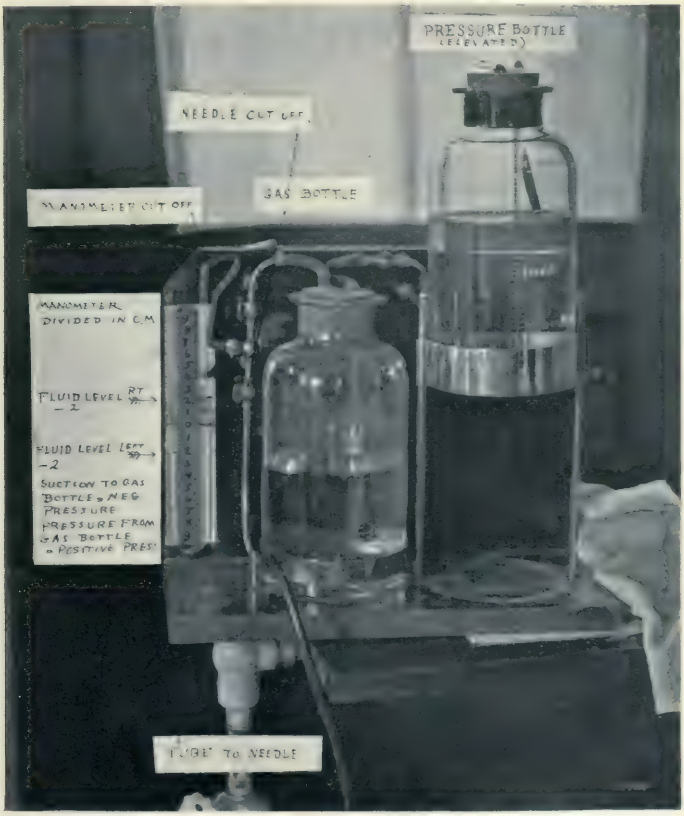

Fig. 247.

reason to fear any bad results from the use of gas, though should we fail to enter or finally be obliged to give it up as useless, the depressing effect upon the patient will be unquestionably very bad. If, as is reasonable to expect, we collapse his left lung in five or six fillings, and keep it collapsed thereafter by refillings for the next six months to two years, it is not unreasonable to

hope that he may be restored to working efficiency within the year, as I have seen happen in a number of cases. Should he not be able to remain under my care the refills can be done at his home by any intelligent physician who will supply himself with the necessary apparatus and follow a strict routine in his procedure. Having then decided to carry out the pneumothorax, I shall proceed to prepare my apparatus. I will place this table near the patient's bed, cover it with sterile towels, and

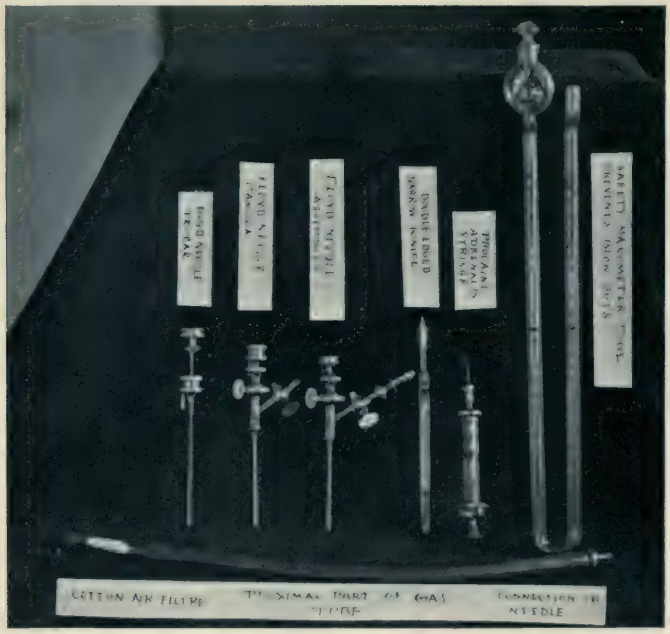

Fig. 248.

place here two basins of solution, one for my hands and one for the cotton sponges, of which we will only need a few. On the corner of the table near the patient, so that if I have no assistance I can reach the gas cocks easily, I will place the gas bottles, so faced that the manometer will be in full view as I work, as a knowledge of its fluctuations is *essential* to safe and sane procedure. An assistant is a great convenience, but is by no means indispensable. On the sterile towels I lay out the needle, that

of Robinson being the one that I have always used and which I have found entirely satisfactory. This needle and the apparatus are made by Codman & Shurtleff, of Boston, by Max Wocher, of Cincinnati, and by other instrument dealers. While there are numerous other arrangements of gas and pressure bottles for the purpose, and the Floyd & Robinson apparatus is only one of many, I have found it extremely handy, easy to carry from house to house, simple to manipulate, and the arrangement of cocks for throwing in or out of connection the manometer or gas tubes is extremely convenient. The arrangement also for raising or lowering the pressure bottle is satisfactory. My only criticism is that the manometer is rather too short, so that if the patient coughs while it is open he will at times blow out the water. A very satisfactory apparatus can be improvised at small cost by any doctor with two 2-liter graduated glass bottles, perforated corks, glass tubing, cut-offs, rubber tubing, and a manometer, but it is usually more convenient to buy the apparatus ready made. I formerly always used nitrogen gas, but various workers, notably Webb, have shown that air is just as satisfactory, and that anyway, after a short time, the gas in the pleural cavity shows the composition of air, so that now, having run out of nitrogen, I have used air with entire satisfaction. I have filled the gas bottle with air by first filling it full of bichlorid solution and then lowering the pressure bottle to start siphonage, letting the air pass through cotton to filter out any dust. Along with the needle I lay out on the towel this small narrow double-edged knife, also this Luer syringe containing 1 or 2 per cent. procain (formerly called "novocain") solution in 1 : 10,000 adrenalin, and have handy another syringe with morphin and strychnin tablets for use in case of necessity. The gas tube and glass-cotton air filter should be dry sterilized, while the water in the bottles should contain 1 : 1000 bichlorid or cyanid of mercury.

In choosing the point to enter we naturally wish to go in where there are as few adhesions as possible, and this demands, of course, a very full knowledge of the percussion and auscultation findings of the lung as well as an *x*-ray plate or a fluoroscopic

examination. There are no very satisfactory means of determining where we will meet adhesions. Sometimes stereoscopic plates are useful and sometimes auscultation will help us, especially where abundant frictions reveal old pleurisy, but I have found percussion my best guide, and have rarely failed to get in where I have gotten a good clear percussion note. Further, it is essential that we be thoroughly informed of the condition of the better lung, so as to be sure it can bear the burden of the double work it will have to take up, and so as to be familiar with its former condition and able to compare it with its condition after the pneumothorax has thrown an extra tax upon it. Where feasible, I find it distinctly best to avoid the popular point of entry in thoracentesis, namely, the ninth interspace below the angle of the scapula, and to enter the needle somewhere between the nipple line and the midaxilliary line, usually in the fifth interspace. When going in on the left side, as in this case, it is very important to be sure that the heart has not been dislocated to the left, as it is by no means impossible, through carelessness, to puncture it, and hence it is a wise practice always to mark the apex-beat before proceeding with pneumothorax. In the case in hand I find normal resonance all over the area between the nipple and the midaxilla, and that the base of the lung has 1 inch of good motion on deep inspiration and the heart apex is in its normal place. In this area I find today a few crackles (pleural?) on cough, as well as a little cog-wheel breathing, which may indicate a slight pleurisy, but probably not enough to hinder the operation. I will now place the patient on his right side with a pillow under it so arranged as to make, if possible, the the chosen point of entry the highest point of the lung, so that our bubble of air will remain there and not tend to travel to some higher point. However, while this is desirable and correct, I have often gotten in easily where it was impossible to raise the point of entry to the highest level. I will next prepare the field which may be rendered aseptic by any of the recognized methods. Personally, I have found green soap, alcohol, and mercuric cyanid solution entirely satisfactory, as it leaves the skin moist and pliable, whereas iodin makes it abnormally dry and harsh. I will

now surround the field with sterile towels and will raise the patient's left hand well over his head both to assist in separating the rib spaces and to leave me a clear field (Fig. 249). Now, with sterile fingers, I feel for the chosen interspace and with a hypodermic full of the anesthetic infiltrate a small area intradermically, then plunge the needle in vertically to the pleura, on which I deposit a portion of the syringe full of the anesthetic, depositing the rest, as I withdraw my needle, in the intervening tissues. In some very nervous patients it may be necessary to use another syringe-

Fig. 249.—Patient in position. Area of formerly injected gas (tympany) shown by skin pencil, also ribs and point of entry. These marks are not used in practice.

ful, and in any case we should let enough time elapse so that the anesthesia is complete and there will be as little pain as possible, as pain makes the patient nervous and makes the operation more difficult. Indeed, where the pain is severe and the patient tends to hold his breath and press down, he may so inflate the lung against the chest wall as to make it impossible to get air into the cavity. When done carefully the procedure is usually entirely painless, though sometimes nervous women complain of suffering a great deal, which suffering,[1] I am satisfied, is much

[1] Note facies of patient in Figs. 251 and 252, showing no pain or anxiety.

more in their minds than in their bodies. I will now take the double-edged knife and make a small epidermal incision, which greatly facilitates the entry of the rather obtuse needle. In cold weather it is wise to place a part of the gas tube in a pitcher of hot water to warm the air or gas. Now taking the needle, holding it as I show you with the top in the palm of my hand and its shank between my thumb, index, and middle fingers, so that its axis of entry will be in the axis of motion of my forearm and its point entirely under control, so that its advance can be stopped

Fig. 250.—Patient and instruments ready. Note method of holding needle, butt in palm of hand, shaft held by thumb, index and middle fingers, giving proper control of advancing point.

quickly, I pass it through the small skin opening, through the intervening tissues, going through the interspace down to the pleura, and if you listen I think you will hear it pop through the fascia or pleura; which of these tissues it is that makes the sound I cannot say, pleura or fascia; both have been claimed by different writers. To me it seems as though it must be a combination of the two. In any case it is usually immediately after we pass this point that we manage to get into the pleural cavity. Before going further let me advise you not to hold your needle, as some do, like a pen, depending upon wrist motion for its entry. It is

much more difficult in this way to stop the advance of the point and you are, therefore, much more apt to wound the lung (Figs. 250 and 251).

As you will observe, I have entered the needle while it was shut off from the manometer, because at times a high negative pressure may draw the fluid out of the tube chestward. My needle point should now be so located that when I open my manometer I will promptly get negative fluctuations of at least

Fig. 251.—Needle has just been entered; manometer reads —2, —6. Gas has been turned on and is flowing easily, hence pressure bottle is not elevated. Needle is steadied at point of entry by index and middle fingers of left hand protected by wet cyanid cotton. Shank held by right hand. Trocar withdrawn and shut off from cannula by cock. It can be reintroduced if needle becomes obstructed.

2 or 3 cm.; smaller fluctuations than this, from $\frac{1}{2}$ to 1 cm., are not to be relied upon as a guide. You will observe that having opened the manometer I get no fluctuations at all. This either means that my needle has not passed the pleura, which I am certain is not the case, since I heard it "pop," or that it is engaged in thick adhesions. I will now push the needle very slowly forward, keeping the manometer open. I note that the needle point does not feel free, and it will be impossible to be sure that I may not puncture the lung. You may notice that I am getting

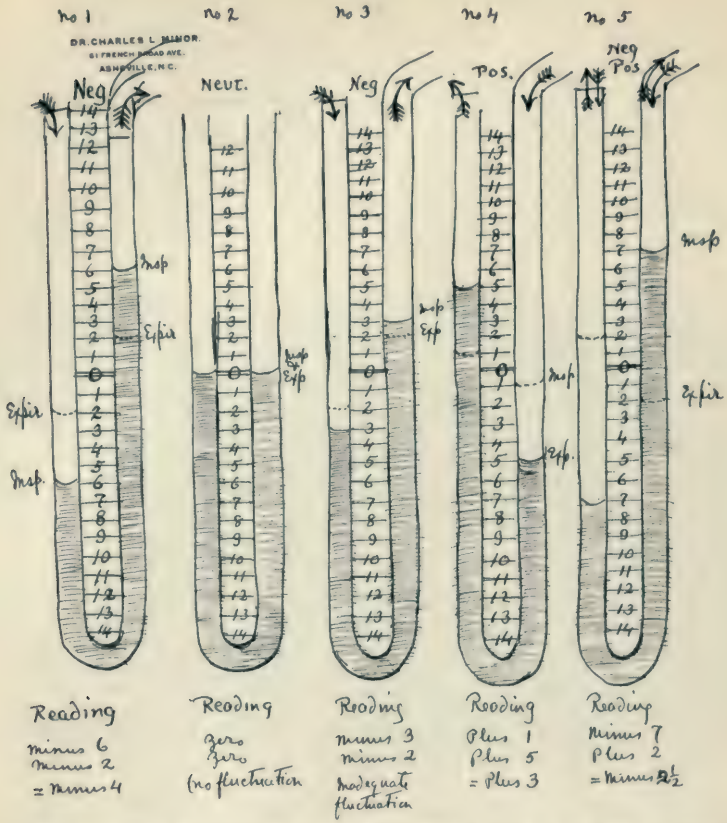

Fig. 252.—The manometer reading indicates the state of suction or pressure within the pleural cavity. One end of the manometer being connected by tubing and needle with this cavity, as long as breathing goes on we have a regular rise and fall of fluid in the two legs of the manometer. When there is a vacuum in the chest we get suction which raises the fluid in the thoracic leg of the manometer and naturally depresses it in the other leg. We read the level of motion at inspiration and expiration, the correct reading being the mean of these two readings. Where by introducing gas into the thoracic cavity we get pressure, we then begin to get positive readings, the fluid being depressed in the thoracic side of the manometer to below the zero point and raised on the other side. Usually in a first injection we get free negative fluctuations running between —9 and —2, showing the existence of a strong vacuum in the thoracic cavity. As the gas flows we get less and less vacuum and suction, until toward the end of the injection we may get a reading, for instance, such as —7 and —4. If reinjections are postponed too long we will find that we get marked negative readings at these reinjections; whereas, if they are spaced wisely, we will still find slight positive or mild negative readings. The

moderate, positive, equal fluctuations and know, therefore, that my needle has gotten into lung tissue. This is unquestionably undesirable, as you may thereby infect the pleural cavity, yet it occurs from time to time and usually has no bad results, though sometimes the patients will spit a little blood immediately thereafter. I have now tried several intermediate points, advancing and withdrawing the needle carefully, and have failed entirely to get proper free negative fluctuations; I will, therefore, remove the needle and seek a better point of entry. I find that more than two trials at entry is apt to make the patient extremely nervous, hence if you fail twice in succession it is best to postpone another puncture to a later date. This point, 1 inch outside the nipple, gives good resonance, the breath sounds here are clear, and, as I have already shown you, the motion of the base, while limited, is not absent, and the apex-beat is not too near. Having prepared the new field, I will take a new sterilized needle, lest the first should have become infected, and prepare for another entry. You will note that the patient winced a great deal at my incision, which proves, I am afraid, that I was rather too impatient and did not give time enough for the procain to take full effect. There is a certain danger in this, as it makes pleural shock much more possible; indeed, if the pleura is always carefully anesthetized, such shock would seldom or never occur. I think that you have again clearly heard the point pass the pleura. I open the manometer, and you now see that I get satisfactory negative fluctuations from -4 to $-6\frac{1}{2}$ cm., and I now feel perfectly safe in opening the gas-cock and shutting off the manometer. Some consider it important to keep the manometer connected with the pleural cavity while the gas is flowing, but if you take readings after each 100 or 200 c.c. of gas has entered, I believe this to be unnecessary, and if left open a sudden

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fluctuations, to be a satisfactory guide, must be greater than 1 cm. In early injections and possibly in any injections it is unwise to produce too great a positive pressure, and we must be content to go cautiously and not to change the pressure too greatly at one time. Incidentally, I might state that the fluid in the manometer should be colored with some dye so that its level can be quickly and easily read.

cough will empty your manometer. At times we get a single high negative rise which remains stationary or falls slowly to zero. Saugman ascribes this to the closure of the point of the needle by contact with the visceral pleura. Watching the level of the fluid in the pressure bottle and observing its relation to the graduations on the bottle, which are in centimeters, you note that the water steadily falls as it presses the gas in the gas bottle into the pleural cavity; 100 c.c. now having entered, I will shut off the gas and measure the pressure. You will observe that the pressure has risen considerably with so small an amount as 100 c.c. of gas, the reading now being -3, -5. This relatively large rise with a small amount of gas would indicate that the space into which the gas is flowing is rather restricted, which may be due to unbreakable adhesions or to slight delicate ones, in which latter case, if I continue to inject gas with some rise of pressure, they will probably break down and the pressure will become more negative. We have now put in 200 more c.c., which makes 300 in all, which is as much as I ever allow myself to put in at a first injection, though it would be easy to inject a much larger quantity. You will note that the patient complained of a slight pain during the injection, and I think you will find that we have broken some slight adhesions. Slight pain during the procedure can be neglected, but severe pain is an indication to stop for that time. Reading the manometer, you note that despite having put in twice as much as at the first flow, our reading is $-2\frac{1}{2}$, $-4\frac{1}{2}$, and I doubt not the gas has burrowed its way through slight adhesions and formed a very decent bubble, else we would have gotten a more marked rise. There is a great temptation to go ahead and put in more, but experience has taught me that it is much wiser for the first time to be content with a small quantity, hence I will now draw out the needle. When I first applied the procedure I followed Brauer's advice and put in as much as 1000 to 1800 c.c. of gas, but as a result caused at times waking up of sleeping processes in the good lung. Since then I have followed Forlanini's rule of not over 300 c.c., and have had no such trouble. Now with a pledget of moist sterile cotton I rub the puncture hole in various directions so as

to assist in the closing of the channel. We will now place a small square of sterile gauze over the puncture and, since the final pressure was not high, will put only a simple adhesive over this. If it were a reinjection and I had used high pressures, with the probability of gas leaking out through the canal and consequent subcutaneous emphysema, I would put a small firm ball of cotton over the gauze at the site of the puncture and strap down firmly on this. This is usually sufficient to prevent leakage. You will note that the patient has had little or no pain and is in perfectly good condition. I find his pulse excellent, and it will not therefore be necessary to give him a hypodermic of morphin. In nervous patients when I have not, as is my habit with them, used it at the beginning of the procedure, I sometimes give it at the end to quiet the patient down for the next few hours and prevent cough, which favors emphysema. After a first injection I prefer to keep the patient quiet in bed all day.

In refills it is usually perfectly safe for the patient to get up at once and go out again on the cure, if he be afebrile, and on exercise, which is rarely the case at first with the patients to whom I apply it, but some authors advocate bed rest in all cases. You will have noted that the gas and pressure bottles in this case I kept upon the same level. This was because it was a first injection and I did not wish to use any very high pressure; but usually it is desirable to raise the pressure bottle so that the pressure of the fluid will make the entry of the gas easier. This is especially necessary where there are many adhesions which we may desire to loosen or where the gas begins to flow in very slowly, showing too much resistance in front; but it must not be forgotten that in the use of very high pressure there is a possible danger of rupture of the mediastinum, with the production of a double pneumothorax. Another great danger of high pressure is the tearing of an adhesion from its lung insertion, thus infecting the pleura and forming a pyopneumothroax. If you will observe the patient you will see that he shows no dyspnea or discomfort of any sort. (See Fig. 251.) Dyspnea is rarely felt after the first injection, but when we use larger quantities later on it is sometimes slightly troublesome and may demand the removal of part of the gas, but

I have never seen any serious results. Gas can be removed by starting siphonage from the pressure bottle, and as the antiseptic solution flows out it sucks out a corresponding amount of gas. A sense of tightness in the chest, however, is usually produced at each injection of gas, and, indeed, the patients are not satisfied after they have had a number of injections until they feel this tight feeling. They seem to feel uncomfortable when they feel "loose," as they call it, and this sense of looseness, with return of cough and expectoration, are our best indications for a refill. Of course, we should not wait for the development of such symptoms, but should so space our refill as to anticipate their appearance. At the first few injections we rarely reach a positive pressure if we have been prudent and gone forward cautiously. At later fillings, however, it is desirable to bring about positive pressures. There are some workers in this line who aim never to pass zero. I myself prefer moderate positive pressure, but do not like to go higher than 4 cm. of water, though some very good authorities (Riviere) have used much higher pressure than this. On the whole, I prefer in refills that my final pressure run between zero and 4 cm. If pressure is not high enough, refilling will become necessary too soon, but if it is too high there are, as I have already stated, certain dangers connected with it, the greatest of which probably is throwing the burden of extra work too suddenly on the other lung, which, you must remember, usually has some foci of trouble in it, and if it is too quickly forced to compensatory action these may very easily light up into activity. High pressure also may, as I have said, rupture the mediastinum or produce troublesome deep or subcutaneous emphysema, which is not a serious complication but a very uncomfortable one, and which also prevents any useful subsequent auscultation. You will note that during the procedure I held the needle at the point of entry steadily by the fingers of my left hand (see Fig. 251), interposing, however, a pledget of wet cyanid cotton between the skin and the needle to decrease the possibility of any infection, and was careful to hold the shaft of the needle by my right hand as immovable as possible, since an excessively small advance or lateral motion will often run the point against some adhesion and stop

the flow, or, what is much more dangerous, may force the point through a distended vein in an adhesion and produce that chief and worst complication of this procedure—air embolism. A wabbling needle point, therefore, is a distinct danger and must be guarded against by a very steady hand, and for this reason it is much better to have an assistant, so you can put all your attention in keeping the needle point still. I would again stress the extreme importance of proper holding of the needle on entry, the butt being in the palm of the hand. This allows great delicacy in advancing and withdrawing the point and gives a certainty of control obtainable in no other way. Should you at any time have the misfortune to enter a blood-vessel, you will find the blood showing itself in the small glass cotton filter tube which you see I have placed in the course of the rubber gas tube, and you will note in the manometer a rapid rise of pressure without fluctuations. If by any possibility you had not observed this and had opened your gas-cock you would very probably have killed your patient. If, on the contrary, the gas is not turned on and the needle is quickly withdrawn no harm will occur. While it is a safe and wise rule never to open the gas-cock until you get distinct negative fluctuations, I have in certain cases violated this slightly when I have been sure my needle was in the right place, and yet when I could get no fluctuations to speak of, by quickly opening and shutting the gas-cock for the fraction of a second. This admits a minute bubble of air and often forces apart the pleural layers sufficiently to give you at once clear fluctuations, and I cannot believe that the very minute amount of gas that is thus introduced can possibly do harm.

In the case I have shown you I expect to follow my usual procedure and renew gas on the day after tomorrow, entering not through exactly the same puncture hole, but in the immediate neighborhood. My third injection I usually give on the fourth day, my fourth after a week, my fifth after ten days, my sixth after two weeks, my seventh after three weeks, my eighth after a month, but, of course, cases vary and no hard-and-fast schedule can be followed in all cases. Sometimes I allow two months to elapse, but usually a month is the longest interval that is safe.

However, I am becoming more and more convinced, with Riviere, that more frequent refills are better and prevent readhesions, and believe two weeks is often wiser than four.

The question of readhesions is one of the troubles of the procedure, and brings not a few cases to an unsuccessful termination after weeks or months of great success. How it occurs I am not prepared to say. One would think that if the collapse had been satisfactory it would be impossible for the parietal pleura to touch and adhere to the visceral, but the fact remains that sometimes after introducing gas with no trouble at all the space begins to get smaller and smaller, it is more and more difficult to get in any gas, and finally the attempt has to be given up as a failure. This may usually be avoided by shorter periods between refills, giving the pleural surfaces no chance to touch and readhere. I have one such case at present that is going down hill, with waking up of the process in the partially collapsed lung where, had I been able to continue to introduce gas, I feel sure that he would have made a complete and satisfactory recovery. For this reason it is not safe to stop the gas for two or three months and then try to recommence. While in some cases this may be perfectly possible, it is frequently a failure for the reasons stated.

When once the lung has been well collapsed, it is often perfectly satisfactory for the patient to take up regular work while continuing to receive injections, and it is reported that certain pneumothorax cases are fighting in the German Army.

You may ask what course I would expect this case to follow if it behaves normally? In a perfectly and properly collapsed lung you will find the temperature drops rapidly, although in some nervous and excitable people there is a slight rise at first, followed by a fall later. The cough and expectoration are temporarily increased, while the patient spits out the sputum which is forced out of the collapsing lung, but this is followed by a remarkable and most satisfactory decrease, and very soon all expectoration ceases. The psychic effect upon the patient of his wonderful improvement is splendid. He feels hopeful and, getting rid of the terrible toxemia in one or two weeks, he feels like a new man. The tiredness which oppressed him disappears, the light of health

comes back into his eyes, he is freed from most of his trying symptoms, and has to be carefully watched lest he become too enthusiastic and foolishly overdo. In a few left-side cases where the diaphragm is pressed down upon the stomach the appetite is affected and dyspepsia produced, but this has not been a frequent, though once or twice a troublesome complication. The promptness of the improvement in many cases is one of the wonders of modern

Fig. 253.—Another case of good compression of left side. Basal and apical adhesions prevent complete collapse, but center part is well compressed toward mediastinum. Heart shoved over to right side.

therapeutics and can be compared to nothing so well as the effects of the successful use of salvarsan. To see a very sick man suddenly changed to one who feels well, to see the racking cough stop, the profuse expectoration, after a temporary increase, disappear, to see the fever fall, the weariness leave him, the eyes brighten—is a very delightful experience to any doctor. In the best cases this improvement continues uninterruptedly until the patient is able to return to his work. In others it is inter-

rupted by certain complications, the most troublesome of which is the collection of fluid. This I have come to look upon as an unfavorable occurrence, although at times fluid takes the place of gas with perfect satisfaction and remains uncontaminated, but in a certain percentage contamination occurs, and when this occurs we have a dangerous complication on our hands.

I have already referred to the readhesion of the lung, a most disappointing complication. One of the saddest things connected with the procedure is the very painful effect upon the patient, who has begun to see health coming back by leaps and bounds, when, through some complication, the procedure has finally to be given up. It is hard, indeed, for the doctor then to make the patient bear it patiently or calmly, and the absolute loss of hope hastens the fatal end.

I failed to note that it is very wise at the end of the operation to map out carefully with the skin pencil the area of tympany which marks out the gas bubble and also to note the displacement of the apex of the heart and of the mediastinum, and to examine the patient with the fluoroscope. At successive refills it is very interesting to watch the fingers of gas push themselves out in different directions between the layers of slightly adherent pleura. One would expect the introduction of the gas would at once prevent the transmission to the ear of any adventitious sounds from the lungs, but it is not always the case, and it is often surprising how large an amount of compression can be brought about before we entirely obliterate such sounds. The reinjections, since there is already existing a good gas pocket, are usually extremely easy, but it is well to remember that air embolism has more frequently been reported at reinjections than at first injections, probably on account of the needle entering a vessel in some adhesion, and therefore we must continue to be as extremely careful as at the first introduction.

This patient must now be kept quietly in bed for twenty-four hours at least even had he been afebrile. Since he was a febrile case he will be kept there in perfect quiet until the procedure has largely freed him from temperature, something which I hope we may anticipate within a week or so.

Subsequent Note (two months later).—The collapse has gone ahead very satisfactorily as far as the lower two-thirds of his lung are concerned. The fluoroscope shows it well compressed against the mediastinum from the base up to the level of the third rib. From this point up to the apex the adhesions have prevented a complete collapse, and it is unlikely it will be possible to break down such dense adhesions, but the patient has benefited greatly, his temperature has ceased, his cough and expectoration, while not all gone, are very much lessened, the toxemia has disappeared, and the general condition is much better. He has gained 15 pounds in weight, though many of these cases lose rather than gain after the operation, probably owing to the lessened area of oxidation. It is very seldom that the lung undergoes a perfect collapse. In one case which I had it was collapsed to the size of a tennis ball, and the shadow protruded from the right side of the sternum between the third and the fifth ribs, the whole of the rest of the pleural cavity being clear. In many other cases bands of adhesions show up very plainly, running out in star-like radiations to the walls and giving butterfly-like shadows. Judging from his present condition this case is going to get a satisfactory result, but, of course, it is impossible for me to say how long I will wish to keep up the reinjections of gas. Many patients never wish to stop, their relief being so great and the terror of relapse so acute that they prefer the monthly reinjections to the chances of a normal expansion, and I can scarcely blame them, for I have seen renewal of activity after such expansion, and usually this means a fatal result. So far we have not data enough to guide us in forming an opinion on this question, but, of course, the ideal will remain a complete re-expansion and resumption of normal function, but many men, from fear of a relapse or at their patient's request, continue refills indefinitely. In this connection the remark of an intelligent medical student who had seen a case which had been under pneumothorax five years seems to me to cover the ground: "It seems to me pathologically unsound to do it, though perhaps it may be clinically correct."

CONTRIBUTION BY JAMES S. McLESTER,
MAJOR M. R. C.

BIRMINGHAM

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CERTAIN MEASURES TO PREVENT THE DISSEMINATION OF DISEASE

WHILE much has been written recently concerning the modifying influence of war upon modern surgery, it will probably be found that we shall also have to revise in a radical manner our works on medicine. The chapter on pneumonia must be entirely rewritten; indeed, we can truthfully say that it has been largely rewritten within the past three months.

It is impossible to discuss here all of the new things which we have learned since the intimate contact of hundreds of thousands in the army camp has offered such fertile fields for the spread of disease. The rapid spread of respiratory infections, the clinical types seen, the high mortality in the post-measles bronchopneumonias, the part played by the Streptococcus hemolyticus, the frequency and the high mortality of empyema with its surprises at necropsy, all are of great interest, but we have had as yet insufficient time for their satisfactory consideration.

From all our rich experiences of the past winter, however, there is one thing which we seem to have learned fully and finally; that is, the value of preventive measures. To me this has been our greatest lesson, and it is of special value in that it is applicable to the civil hospital as well as to the armed camp. If we are to prevent the spread of respiratory and other contagious diseases three measures are necessary: (1) the avoidance of overcrowding; (2) the universal use of the cubicle method of isolation; (3) the employment of masks for patients and attendants.

Pneumonia is the one disease that we fear most and toward which preventive measures are chiefly directed, but the same means which will prevent the spread of this disease are applicable also to scarlet fever, meningitis, diphtheria, measles, influenza, tonsillitis, and many other diseases. In fact, when we consider the "droplet" as a means of disseminating these diseases, we come to wonder how great a proportion of all bacterial invasions occur in this manner, and are tempted to extend widely the application of our preventive measures.

The necessity for ample floor space between beds and for plenty of air is obvious. In the Base Hospital at Camp Sheridan we have escaped the great pneumonia epidemics which some of the camps have experienced, and all types of pneumonia seen by us have been mild, with a relatively small incidence of empyema. We have attemped to explain this fortunate circumstance in various ways, but after comparing our experience with that of certain other hospitals I am convinced that the ample floor space which we have been able to allot each patient, and our consequent escape from overcrowding, have been the most important factors. We have endeavored always, particularly in pneumonia, measles, and scarlet fever, to provide 1000 cubic feet of ward space for each patient.

The soldiers with acute lobar pneumonia have been placed on the veranda, with universally good results, and many of the patients with bronchopneumonia following measles or influenza have also been treated in the open, but there seems to us to be a difference in the way in which these two groups of patients take the "open-air" treatment. During cold, disagreeable weather the patient who has developed bronchopneumonia as a sequel to bronchitis or measles certainly seems very miserable and unhappy on the veranda. It is difficult to make him comfortable and his cough is at times very annoying. The explanation of this difference may be sought in the fact that the one is suffering with a disease of the lung, pure and simple, and the other, in addition, has an irritable upper respiratory tract. We have become convinced that the open-air treatment can sometimes be carried too far, and that for certain patients ample space in a well-ventilated ward during the winter is frequently to be preferred.

The space allowed each patient should never be less than 1000 cubic feet, and continuous free ventilation of the entire ward should be assured. This is a measure of infinite importance.

The surgeon general directed early in the winter that the cubicle system of isolation be adopted in those wards in which patients with contagious diseases were being treated. Wires were stretched across the entire width of the ward, $6\frac{1}{2}$ feet from the floor, between the beds, and sheets were hung upon these wires in such a manner as to isolate each bed in a sort of cubicle. The space below and above the sheet permits the free movement of air, but no patient can by talking, coughing, or sneezing throw his bacteria-laden droplets of moisture to the bed of his neighbor. The evident effect of this barrier in preventing the transference of disease from one patient to another offers eloquent testimony as to the great rôle played by the droplet in spreading contagious diseases.

In certain instances the influence of the cubicle was remarkable. At a time when we had a ward full of patients suffering with measles, and everybody was coughing and sneezing, respiratory infection was almost universal among these patients. True, as soon as a case of bronchopneumonia was recognized the patient was transferred to another ward, but in spite of this precaution the dreaded complication increased. Finally, more room was provided for the individual patient, and each bed space was converted into a cubicle. The coughing and sneezing immediately ceased and the bronchopneumonia disappeared. The transformation was graphic. This marked the end of bronchitis and pneumonia as a dominating factor in the measles ward, and the lesson is not easily forgotten.

In April we were overtaken by an epidemic of so-called influenza, and the number of patients in the hospital suddenly increased from 400 to 900. It became necessary to place these soldiers in wards with patients suffering with other affections, and these latter began rapidly to come down with influenza. Because of this we then decided to extend the cubicle system to all the medical wards without exception, and the beneficial effect of this measure was immediately felt. As illustrative of its influence, take our experience in a certain ward. Not until late

in the epidemic was it necesssary to place any of the grip patients in the psychopathic ward, at which time we had already instituted the general use of the cubicle, and as a result, contrary to our earlier experience in other wards, none of these psychopathic patients developed influenza.

The hospital of the future, both civil and military, must make provision for the protection of its patients by placing every bed in a cubicle. It may be that fixed partitions or movable screens will be found preferable to sheets hung upon wires, but some such system will come. Another winter in the base hospital will, I believe, find all the medical beds in cubicles.

One more means of protection has been found of real value. The wearing of masks by physician, nurse, attendant, and patient. It has been our custom to require masks of physicians, nurses, and attendants in all contagious wards, but the experience of Capps at Camp Grant has caused us to extend this measure to all patients under quarantine who are out of bed. A certain "miscellaneous" ward, for instance, is quarantined because of the appearance among the patients of a case of scarlet fever or diphtheria. Everybody knows how frequently the period of this quarantine must be repeatedly extended because of the appearance at intervals of still other cases, but such "cross-infection" can be entirely eliminated if Capps' suggestions are followed, and each patient wears a mask when out of bed except when alone in the toilet or bath. I am sure that by means of the mask we have limited the complications in our contagious wards.

The mask consists of two layers of gauze cut square, with a piece of tape sewed at each corner, and is sufficiently large to protect the nose and mouth. In this recent epidemic I wore a mask constantly when making the rounds of all wards, and it is the first time I ever passed unscathed through a grip epidemic. Other officers had a similar experience. For my own protection I would not today think of examining a pneumonia or a meningitis patient without a mask, and if none were at hand would protect my nose and mouth with a handkerchief.

The value of these preventive measures has been forcibly borne in upon me, and I write of them here because of their importance to the hospital of the city as well as of the armed camp.

CLINIC OF DR. BRYCE W. FONTAINE

MEMPHIS GENERAL HOSPITAL

A CASE OF ACHONDROPLASIA

History.—White man. Age thirty-four. Telegraph operator by occupation. Height, 51 inches. Weight, 100 pounds. Admitted to hospital because of nausea and vomiting which he says has existed for five days. Temperature, 98.4° F. Pulse, 90.

Physical Examination.—Thoracic viscera negative. Abdomen shows slight tenderness over epigastric region. Blood: Leukocytes, 8000. Differential count normal. Urine negative. The condition for which this patient enters the hospital is an acute gastritis which has resulted from imprudent eating, and is uninteresting to us compared with the man's physical [illegible] ment. Mr. A., examine this man's body and limbs, and tell us what you think of his physical development.

MR. A.: I find that the man is a dwarf; that he has a normal head, has an expression of intelligence, has a trunk of normal proportions, has normal sexual organs, but has very short arms and legs.

DR. FONTAINE: What would you call such a condition as this?

MR. D.: Cretinism.

DR. FONTAINE: That is exactly the answer I hoped you would give, because these cases are nearly always mistaken for cretinism. Mr. D., in what way do you think this man resembles a cretin?

MR. D.: In his size.

DR. FONTAINE: In this I think you are mistaken, because most achondroplastics are taller than the average well-developed cretin. An achondroplastic may, however, resemble a cretin, but the mistake arises from the mere fact that he is a dwarf.

Fig. 254.—Achondroplastic compared with man of average size.

Fig. 255.—Trident hand.

Examine this man's appearance in bed, and you will note that he has an expression of intelligence upon his face; a cretin has the expression of an imbecile. His mouth is closed; a cretin has a wide open mouth, and it is usually drooling with saliva. Feel his scalp, and you will find that his hair is soft like that of a nor-

Fig. 256.—Roentgenogram of humerus, showing enlarged ends and narrowed shaft.

mal man, instead of being stiff and bristly, as is always the case in a cretin. Finally, if we could compare him with a cretin, we could see the uniform dwarfness in the cretin, or, in other words, the trunk as well as the limbs is underdeveloped. Mr. T., is there another condition which might be mistaken for this disease?

Mr. T.: I do not know.

DR. FONTAINE: Yes, two other diseases, rickets and osteogenesis imperfecta. Rickets in its ultimate results usually de-

Fig. 257.—Roentgenogram of forearm, showing abnormal curving of radius, with enlarged ends of radius and ulna.

Fig. 258.—Roentgenograms of hands.

forms and dwarfs the victim until, at first sight, he looks very much like an achondroplastic. The distinguishing features are,

however, that all the bones of the body are affected in rickets, the ribs, head, spine, and pelvis. The long bones are usually much more deformed, bent, and twisted out of shape than those of an achondroplastic. In cases where the diagnosis is difficult we can always distinguish the two conditions by means of roentgenograms.

Fig. 259.—Roentgenogram of foot.

Osteogenesis imperfecta occurs so rarely that it need not give us much concern in the differentiation. This peculiar disease results from imperfect ossification of the long bones, and, as a result, repeated fractures of the limbs occur, causing dwarfness and deformity. It is very rare for cases of osteogenesis to survive

until adult life, and in the few cases that do, the roentgenogram will clearly show the line of fracture and union in the long bones, thus differentiating it from other conditions.

Here we have a dwarf with the peculiar development of achrondroplasia. The photograph of the patient shows his size as compared with a man of average height. A striking characteristic of the disease, in addition to the short limbs, is the presence of short chubby fingers, all of the same length, and the abnormal separation of the ring and middle fingers, constituting what has been termed the "trident hand" (see Fig. 255).

Examination of the roentgenograms of the long bones shows the diaphysis and epiphysis broadened and more plump than normal, and the middle of the long bones correspondingly narrower. The normal curves are all exaggerated. Roentgenograms of the hands and feet show the same broadening at the ends of the small bones.

The etiology of this disease is as curious as it is interesting after it has developed. It has been known to have presented a family characteristic. Males are more frequently affected, and it occurs as a result of some developmental disturbance during fetal life, causing a premature closure of the epiphyses.

The disease bears no relation to syphilis, rickets, or any disturbance of the ductless glands, and is absolutely unaffected by any medical treatment.

TUBERCULOSIS OF THE PERITONEUM

CASE I.—Patient W. S. Male. Negro. Age twenty-four; 5 feet 6 inches tall. Weight, 130 pounds. Occupation, laborer.

Chief Complaint.—Distention and pain in abdomen, some nausea, vomiting, and dyspnea.

Present Illness.—Began six weeks ago, with pain in abdomen, lasting a few minutes at a time, but continuing both day and night. Within the last week patient has lost flesh and strength, has had fever and anorexia.

Previous History.—Negative. Habits good. Ordinary diseases of childhood. Denies venereal diseases.

Family History.—Negative for tuberculosis.

Physical Examination.—Body well developed, poorly nourished.

Eyes.—Sclera and conjunctiva bile-tinged. Mucous membranes anemic.

Throat.—Negative.

Tongue.—Thick frosty coat over dorsum.

Teeth.—Caries and pyorrhea.

Heart.—Apex-beat in fifth interspace, 9½ cm. from median line. Heart sounds clear throughout. Pulse regular.

Lungs.—Normal vesicular breathing throughout. Percussion note resonant throughout. A few small crackling râles can be heard over base of right lung posteriorly.

Abdomen shows distention of moderate degree, circumference at umbilicus 100 cm. Percussion shows tympany in upper part about umbilicus, dulness in flanks. Fluctuant wave distinct. Patient in sitting posture shows flatness in lower part of abdomen as high as umbilicus, tympany above. Palpation of abdomen elicits distinct tenderness, and in several areas there can be felt masses of varying size and shape. Because of the ascites it was impossible to palpate the liver or spleen.

Muscles.—Soft and flabby. Lymph-nodes not palpable.

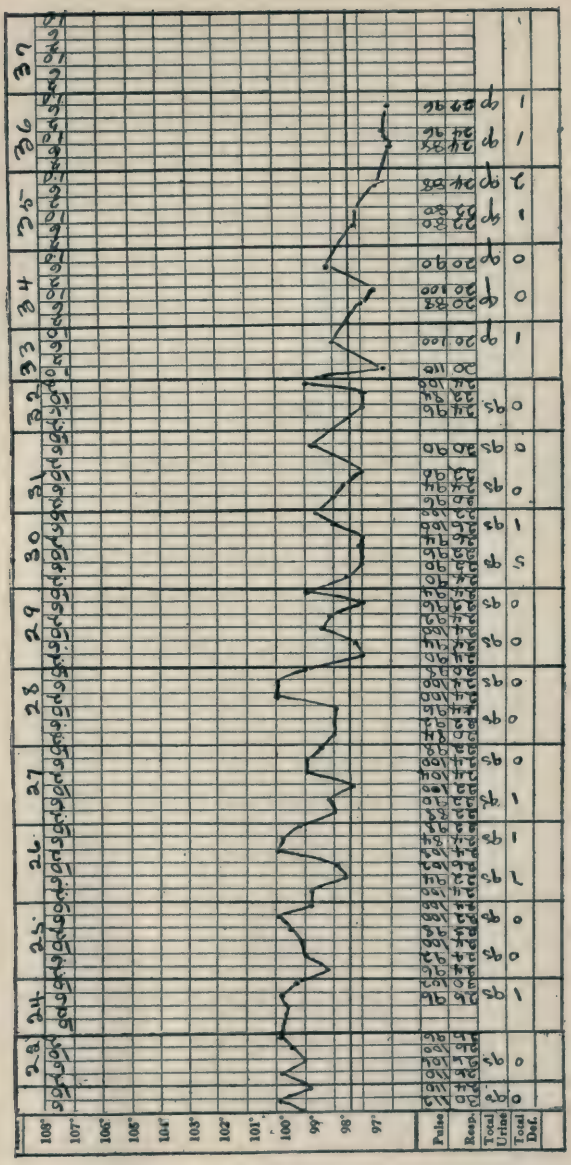

Fig. 260.—Temperature chart of Case I.

Laboratory Examinations.—Sputum negative. Wassermann negative. Urine shows a heavy trace of albumin, and micro-

scopic examination showed numerous hyaline casts, leukocytes, and pus-cells.

Blood.—Total leukocytes, 10,800. Differential count normal.

Gastric Contents.—One hour after Ewald meal show free HCl 22, total acidity 30; no lactic acid; no occult blood. Microscopic examination negative.

Temperature.—Examination shows a temperature curve which is septic in character, in that in each twenty-four hours it reaches almost to the normal, and within a few hours there is a rise of three or four degrees.

The diagnosis of tuberculosis of the peritoneum was based upon the patient's being a young adult negro, with a disease of rapid onset, ascites with tenderness of the abdomen, discovery of masses of thickened peritoneum and mesentery, and the peculiar temperature curve. Because of the temperature curve we could not avail ourselves of the tuberculin test, unless, perhaps, we had relied upon a focal reaction, *i. e.*, increase of pain and tenderness in the abdomen, and not upon a rise of temperature.

The case was referred to the surgeon, with a request for exploratory laparotomy. The following report was returned:

Median incision under local anesthesia. Peritoneum exposed, shows much thickening. Incised, escape of considerable straw-colored fluid. Examination of intestines shows walls thickened and hyperemic, and covered with tubercles varying in size from a pin-head to a match-head.

CASE II.—G. S. Negro. Female. Age forty-three.

Chief Complaint.—Enlargement of abdomen, pain, and tenderness.

Present Illness.—Began six weeks ago with nausea, vomiting, and pain in abdomen. For last four weeks confined to bed because of enlargement of abdomen and pain.

Previous history negative. *Family history* negative.

Physical Examination.—*General Appearance.*—Well developed and well nourished. *Eyes:* Sclera and conjunctiva slightly jaundiced. Slight hyperemia of vessels. *Tongue* clear. *Teeth* in fair condition.

Heart.—Apex-beat in fifth interspace, 9 cm. from median line. Heart sounds clear. Pulse rapid, 90 per minute. Regular and full volume.

Lungs.—Negative throughout. Respiration is slightly increased.

Abdomen.—Distended; 89 cm. in circumference at umbilicus. Dome shaped. Tympany about umbilicus, dulness in flanks. Dulness changing with position. Fluctuant wave distinct. No masses to be felt, but abdomen distinctly tender all over upon palpation or percussion.

Liver and Spleen.—Not palpable. Skin dry and harsh.

Joints.—Right knee flexed, impossible to extend. Other joints normal.

Lymph-glands not enlarged. Temperature septic in character.

Laboratory Examination.— *Urine* negative.

Blood.—Leukocytes 5400. Hemoglobin 80 per cent. Differential count normal. No malarial parasites. Wassermann negative.

Pelvic examination showed mass, irregular in shape, firm, nodular, size of fetal head.

The diagnosis in this case was based upon the acute onset of the ascites, rise of temperature, and tenderness of the abdomen. As in the case previously reported, we could not avail ourselves of the tuberculin test because of the temperature, and we did not care to produce a focal reaction because of the existing discomfort of the patient.

The patient was referred to the surgeon for exploratory laparotomy, and the following report was returned:

General Anesthetic.—Abdomen contains considerable straw-colored fluid. Peritoneum, intestines, and uterus covered with small pearly tubercles. Uterus contains large fibroid.

In the study of tuberculosis of the peritoneum we are aided very much by the knowledge of the predisposition of the negro race to all varieties of tuberculosis. I think an analysis of our cases for the past five years would show full 75 per cent. of the cases have been in the negro race.

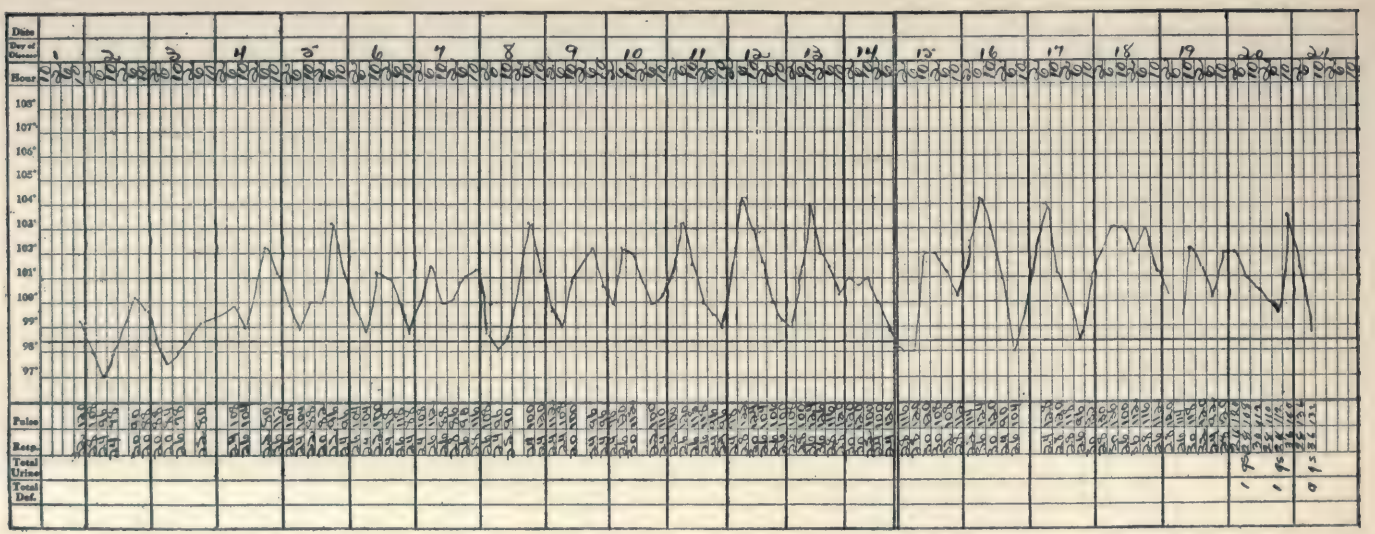

Fig. 261.—Temperature chart of Case II.

We should in all of these cases pay especial attention to the occurrence of local tuberculosis elsewhere in the body in deciding upon the presence or absence of the disease in the peritoneum. Quite frequently there is a history of glandular tuberculosis, or masses in the neck, as negroes usually call them, or a history of pleurisy, or a disease of the hip-joint.

In the case of the female we should never overlook the fact that the fallopian tubes are frequently the starting-point of a peritoneal tuberculosis, and where there is any doubt, a careful pelvic examination by a competent gynecologist might be the means of clearing the diagnosis.

Too much stress cannot be laid upon the study of the fluid obtained through the aspirating syringe, or the study of all of the fluid obtained after a paracentesis. A very difficult and tedious process is the centrifugation of quantities of the fluid, and staining the sediment by the antiformin method, for tubercle bacilli. While this measure is difficult and time-consuming it is possible for tubercle bacilli to be demonstrated.

A study of the cells in the centrifugate will usually show a relative increase of lymphocytes, and while very suggestive of tuberculosis, absolute reliance cannot be placed upon it as a diagnostic sign because the same findings may occur in cancer or syphilis of the peritoneum.

Attempts to cultivate the tubercle bacillus from the fluid are difficult and too slow to be of any value as a quick diagnostic sign.

Inoculation of small quantities of the fluid into the peritoneal cavities of guinea-pigs is a procedure of great value, but objected to chiefly because of the length of time required to produce the disease in the lymphatic glands of the animals. Quite recently it has been suggested that the susceptibility of guinea-pigs could be increased, and the length of time for the development of tuberculosis in them much shortened by exposure of healthy animals, before inoculation, several times to the Roentgen rays.

As was mentioned in the history of both cases, because of the fever that usually prevails, complete reliance cannot be placed upon the subcutaneous test with old tuberculin. Usually, how-

ever, when the proper dose is given there is, coincident with the rise of temperature, a focal reaction which is indicated by increase of pain and tenderness of the abdomen, usually accompanied with nausea and vomiting. The focal reaction is of great value in many of the cases. There is some doubt as to its absolute harmlessness, but it may be necessary as a final resort to clear up cases which are difficult to diagnose.

SYPHILITIC FEVER

In spite of the fact that attention has been called to the occurrence of fever of long duration during the secondary and tertiary stages of syphilis since 1732, and quite recently in the articles of Janeway, Edwards, Herman, and Riesman, it is not unusual for the disease to be overlooked, and for the cases to be treated for long periods under the mistake that they are typhoid fever, malaria, or tuberculosis.

This mistake would occur less frequently if we would remember the great prevalence of latent syphilis. According to Symmers and Whitney, in an analysis of several thousand cases, during life and at autopsy, which were studied at the medical clinics in two large cities, over 6 per cent. showed unmistakable signs of syphilis. The recognition of latent or visceral syphilis will not be overlooked with anything like the frequency that it has been in the past, since the adoption of a routine Wassermann test on all patients entering the dispensary services or hospitals, as is now the rule in most large cities.

The fever that prevails in these cases usually assumes the type of a septic or remittent temperature, occurring either over long periods, in some cases for several months, without a decline, or occurring for several weeks at a time with intervals of normal temperature, for a few weeks, with many recurrences. In the majority of cases the rise of temperature is associated with chills and sweats, and in some cases the chill, fever, and sweat occur at regular intervals, markedly resembling the periodicity of malaria.

In spite of the prolonged fever, as I have observed in two recent cases, the general condition of the patient continues surprisingly good. There is nothing like the emaciation or weakness you would expect in a case of tuberculosis, and the chief and only complaint is the fever, which they are powerless to control.

In most of the cases syphilis has prevailed as a visceral manifestation, and the pyrexia has resulted from the absorption of

toxins that have been brought about by the breaking down and healing of minute foci or even a gumma in the liver. In other cases there has existed a hepatitis, and in one case reported by Edwards there was an undoubted pylephlebitis.

While the liver is the organ most often responsible for the prolonged fever of syphilis, it would be possible for the pyrexia to occur as a result of minute gummata or infiltrations in the spleen, lymph-glands, and even in the gross nervous structures.

The diagnosis is usually made from the fact that the cases do not respond to treatment for ordinary conditions that commonly produce prolonged temperatures. For example, in the cases reported, the first was mistaken for paratyphoid fever, and the second for malaria. These cases are usually kept under observation so long that they wear out themselves and the attendant, and finally are discovered through the means of the Wassermann test, or by the rapid and complete recovery under antisyphilitic treatment.

CASE I.—Male. White. Age twenty-three. Occupation laborer.

Chief Complaint.—Chilly sensations, fever, headache, pain in bones, general malaise.

Present Illness.—Began February 13, 1917, with aching in limbs and back. Chills occurred at frequent intervals, followed by fever and an occasional sweat.

Previous History.—Twenty or thirty cigarettes a day. Moderate drinker of beer and whisky. Denies venereal diseases. No previous illnesses of any description.

Family history negative.

Physical Examination.—Well developed and well nourished. Eyes normal, react to light and distance. Mucous membranes normal. Tongue heavily coated on edge. No tremor. Teeth in fair condition. Gums normal. Throat: Slight soreness and hyperemia of tonsils and pharynx.

Heart.—Apex-beat in fifth interspace, 3½ inches from median line. Heart sounds clear throughout.

Lungs.—Resonant, and normal vesicular breathing without any adventitious sounds, throughout both lungs.

Abdomen.—Distended and slightly tympanitic. A little soreness in right iliac region, a little gurgling upon deep palpation.

Liver.—Not enlarged to palpation. Percussion difficult because of distention of abdomen.

Spleen.—Enlarged, three fingerbreadths below costal margin.

Kidneys.—Not tender or palpable. Skin hot and dry. Bones normal. Joints normal. Reflexes normal. Sexual organs negative. Temperature 102.3° F. Pulse 96, regular and moderately full volume.

Laboratory Examination.—Urine examined at frequent intervals showed an average specific gravity of 1025, and occasional trace of albumin, never any sugar. Microscopic examination showed no casts, a few pus-cells, and bacteria. Diazo test made once was negative.

Blood.—Several leukocyte counts were made. The highest recorded was 13,600; the lowest, 8140. The differential count usually showed a normal proportion of the various types of leukocytes. The blood was specially stained for the malarial parasite, with both the ordinary smear and with thick films, with negative report for plasmodia. A blood-culture made twelve days after entrance and carefully incubated showed no growth. Widal tests with the typhoid bacillus were made at intervals of four days for the first six weeks, and in each instance a negative report was returned. April 24th a Widal was made with an undetermined organism supposed to be one of the paratyphoid organisms, and a positive reaction was reported. There is, however, no note made of the dilution or of the time limit.

Sputum.—Cough was present, and upon several occasions the patient expectorated sputum. Careful examination was made for tubercle bacilli, but upon five different occasions the result was negative.

At this stage of the man's illness the condition was still considered an atypical typhoid fever, but there was a very strong conviction that it might be a case of miliary tuberculosis. Accordingly, an ophthalmologist was asked to examine the eye-grounds. He submitted the following report March 3, 1917: Eye-grounds show an elevation on the central vein in disk of

right eye suggestive of a tubercle. This information apparently confirmed our suspicions, and we redoubled our efforts to find a focus, or to find signs of the disease in other organs. We were also prepared for an early exit of the patient.

In spite of many physical examinations we could never find anything definite in the lungs or other viscera. The patient continued in the same way, with the septic temperature, but without any other definite symptoms.

During the course of the illness the patient was repeatedly questioned as to the existence of syphilis, but he always strenuously denied it. Furthermore, there were no signs of the effects of the disease upon the skin, bones, or glands. In desperation to arrive at a diagnosis, a Wassermann test was made on April 24th, and a 4 plus reaction was the report from the laboratory. Treatment with small intravenous doses of salvarsan, at weekly intervals, was begun at once. Improvement in every way was noticeable after the first dose, and within ten days the patient was afebrile. He was in a short time dismissed from the hospital with a complete and uneventful recovery.

Close scrutiny of the temperature chart will show it is unlike the normal temperature chart of a typhoid or a paratyphoid fever, and that it conforms to the type of septic temperature. At many places throughout the course the temperature has declined to 99° F., but within a few hours it will be seen to have risen to 102° or 103° F. A very confusing feature of the case is the fact that a positive Widal reaction was obtained two months after the beginning of the illness, with a strain of the paratyphoid bacillus. I did not see the results, and personally doubt its genuineness.

At any rate, the patient presented an undoubted 4 plus Wassermann, and did not improve in the slightest way until he was given salvarsan, with the result of a rapid and complete recovery.

Case II.—J. L. White. Male. Age fifty-nine. Railroad man by occupation.

Chief Complaint.—Chills and fever.

Previous History.—Usual diseases of childhood. No serious

illnesses of any consequence. Syphilis at thirty years of age. Treated by usual methods at that time for three years. From twenty to thirty years of age drank moderately of alcoholic liquors. Since thirty years of age total abstainer. Moderate smoker. Ten years ago injured in railroad accident, concussion of brain, which kept him away from work for eleven months.

Present Illness.—Began November, 1916, with what was supposed to be nervous breakdown from overwork. Had severe pain in back, malaise, and physical exhaustion. Kept away from work forty-five days. Returned in fair shape, but still not up to normal condition in weight and strength. April 18, 1917, began to have chills and fever. Paroxysms occurred every second or third day with considerable regularity. In beginning chills were dumb, simply manifesting themselves as cold spells, not accompanied by shaking. Soon after chilly feeling temperature would rise to 102° or 103° F., followed by a sweat. Between paroxysms patient felt entirely normal.

These paroxysms of chills, fever, and sweats continued for one month. Blood was examined many times for the malarial parasite, always with a negative result. In spite of negative findings patient was given large doses of quinin by mouth and intramuscularly without any effect whatsoever.

In July the paroxysms began to recur, the cold spell usually coming on in the afternoon, followed by a rise of temperature sometimes to 104° F., usually followed by a light sweat. These paroxysms markedly simulated malaria, and even though repeated examinations of the blood, by means of ordinary and thick films, with reliable stains, failed to show anything, it was hard to convince one that the condition was not malaria. The patient continued in the same condition until November, 1917, when he consulted the writer.

Physical Examination.—White man, well developed, fairly well nourished.

Eyes.—Pupils equal, react to light and distance. Conjunctiva slightly bile-tinged. Mucous membranes normal. Teeth: Considerable crown and bridge-work. Gums show severe pyorrhea. Throat and nose normal.

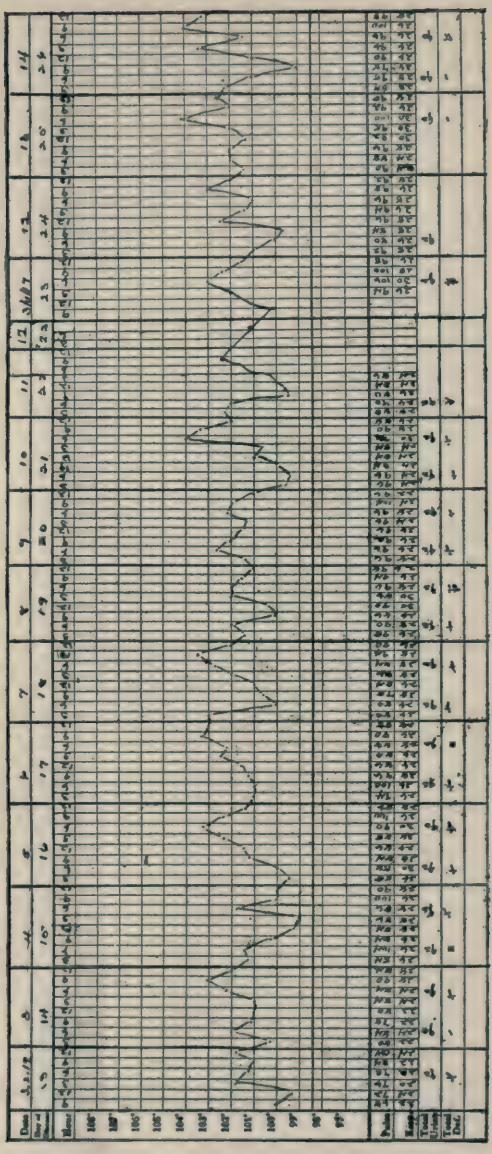

Fig. 262.—Temperature chart of Case II.

Heart.—Apex-beat in fifth interspace, 9 cm. from median line. Second sound in aortic area slightly accentuated. Heart sounds clear elsewhere.

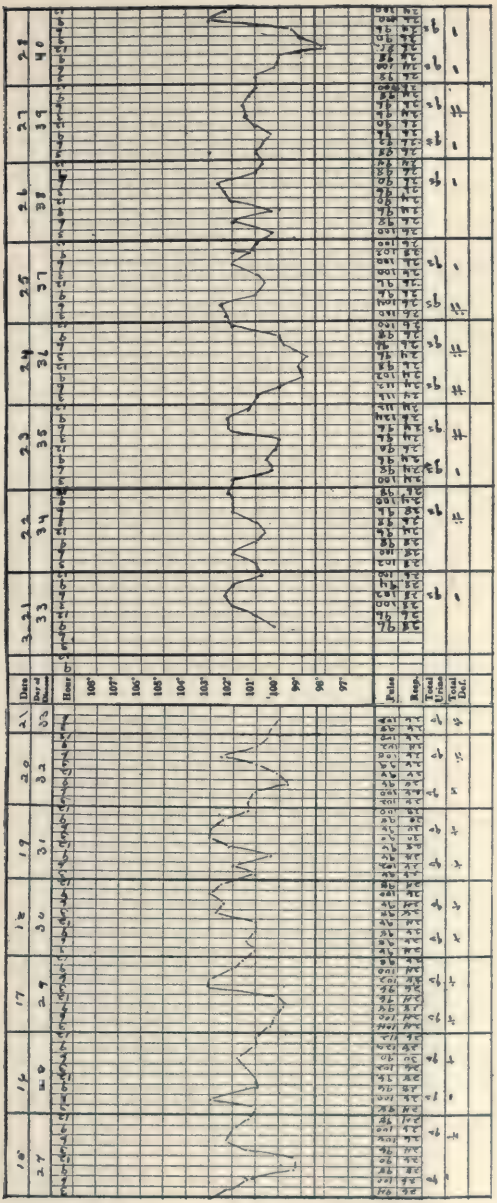

Fig. 263.—Temperature chart of Case II (continued).

Lungs.—Resonance throughout both lungs, anteriorly and posteriorly. Vesicular breathing throughout both lungs.

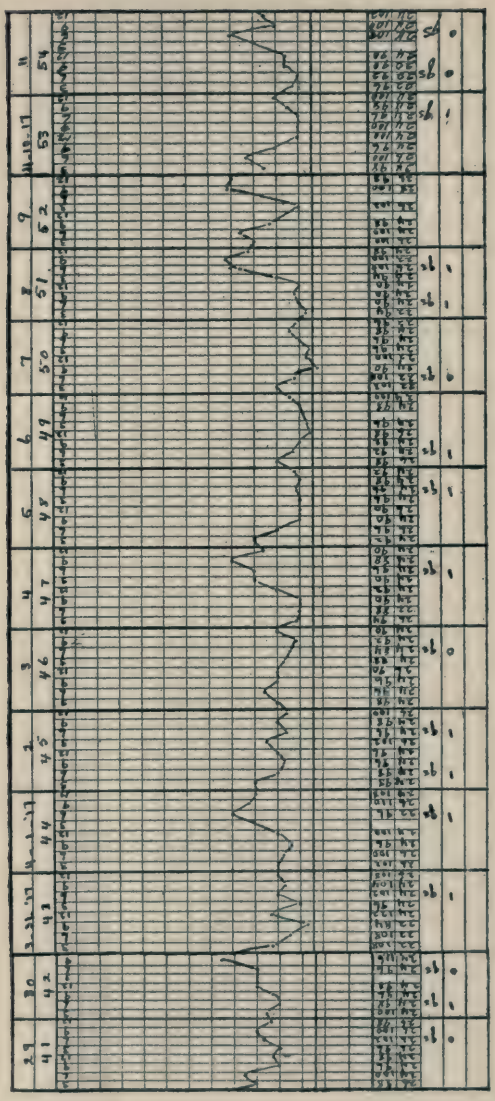

Fig. 264.—Temperature chart of Case II (continued).

Abdomen.—Spleen not palpable. Liver enlarged. Upper border normal. Lower border crosses midabdominal line at least 3 cm. below midpoint between base of ensiform and umbilicus.

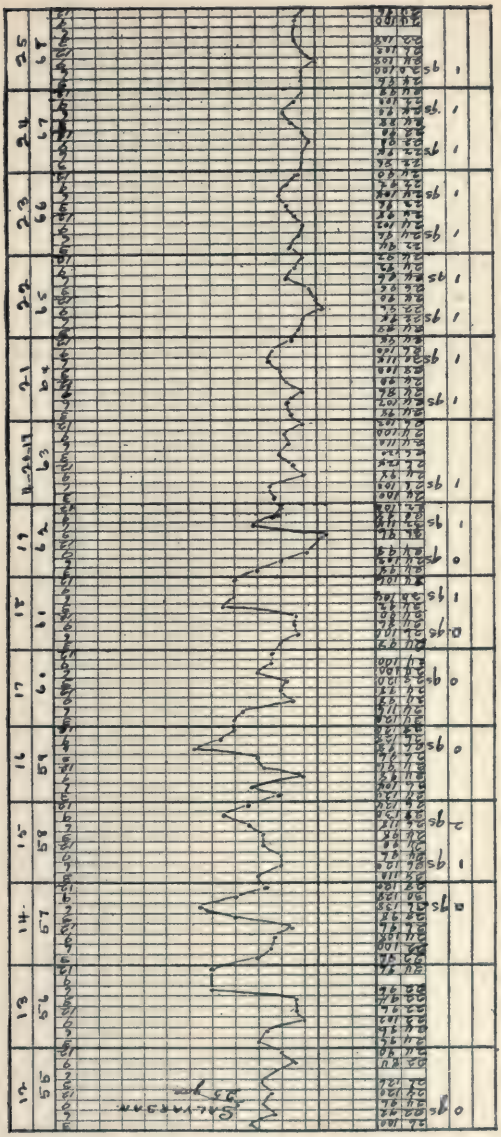

Fig. 265.—Temperature chart of Case II (continued).

Liver slightly tender to forcible percussion and deep palpation. Abdomen not distended nor tender upon palpation elsewhere.

Reflexes.—Patellar active. Gait normal. Joints and bones

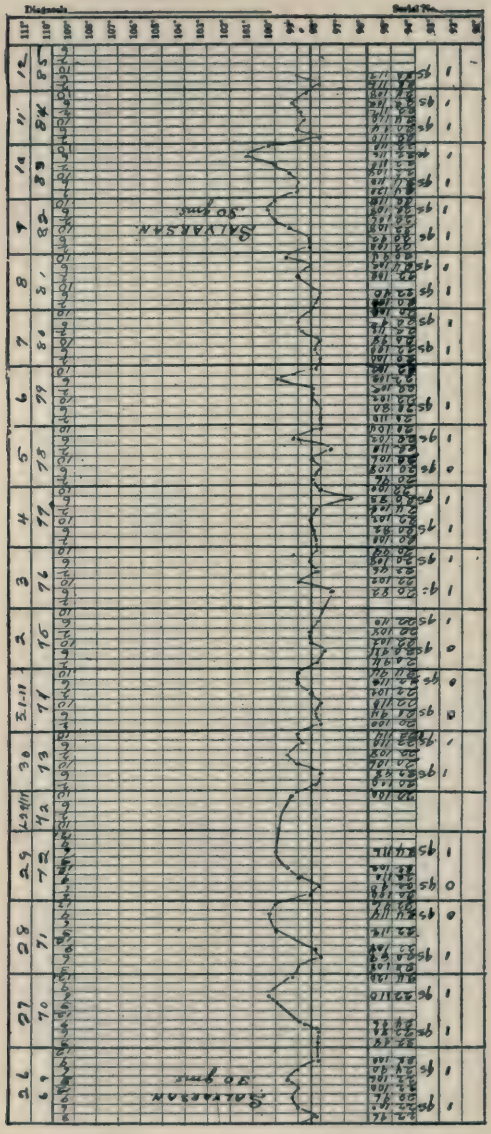

Fig. 266.—Temperature chart of Case II (concluded).

entirely negative. Glands not palpable. Blood-pressure, systolic 140, diastolic 80.

Roentgenogram of chest showed heart normal in size. Aorta normal. Lungs and pleura clear.

Laboratory Reports.—Urine examined many times. Report December 12, 1917: Acid in reaction. Specific gravity, 1014. Albumin, trace. Glucose, negative. Indican, moderate trace. Bile pigment, negative. Diazo, negative. Russo, negative. Microscopic examination shows moderate sediment containing few epithelial cells from lower genito-urinary tract, a few hyaline and pale granular casts.

Blood always negative for plasmodia. Count made December 12, 1917: Erythrocytes, 4,300,000; hemoglobin, 70 per cent. (Dare); leukocytes, 12,800. Differential count: Polymorphonuclears, 77 per cent.; transitionals, 5 per cent., lymphocytes, 10 per cent.; large mononuclears, 8 per cent.; eosinophils, 0; mast cells, 0. Wassermann negative. Widal test with typhoid bacillus, dilution 1 : 50, time limit one hour, showed no agglutination. Test repeated twice, with negative results.

Gastric Analysis (Dec. 20, 1917).—Ewald test-meal. Contents removed in one hour:

Amount, 48 c.c.
Reaction acid.
Color normal.
Free HCl, 30.
Total acidity, 40.
Combined HCl, 10.
Organic acids, 0.
Lactic acid, negative.
Occult blood, negative.
Microscopic examination, negative.

Roentgenogram after barium meal in ten minutes showed a normal Bishop's cap. In one hour no filling defects, normal peristaltic waves. Stomach cow-horn shaped, in normal position. Six hours, stomach entirely empty. Eight hours, barium entering cecum and ascending colon.

In view of the fact that the patient had a severe pyorrhea, a dentist was called into consultation. Roentgenograms were made of the teeth, and several granulomata were found at the

roots of the molars. The dentist advised that all the teeth should be extracted because of the severe pyorrhea and several granulomata. He assured the patient that the temperature was due to the septic condition of the mouth. December 20th, under gas anesthesia, all of the teeth were extracted. The gums were treated antiseptically, and healed in due time, without the slightest influence upon the temperature, the paroxysm occurring regularly every second or third day, just as it had been doing for the past two months.

In January the patient was seen in consultation with a surgeon. A careful examination of the patient's body was made in the hope that a focus of pus could be discovered. Special attention was paid to the prostate gland and seminal vessels. No evidence at all of any trouble was discovered, except slight prostatic enlargement which usually occurs in a man of that age. At the surgeon's request the patient was observed by him for several days. Finally, it was decided by the surgeon that the cause of the temperature was either about the liver or in the gall-bladder. This seemed incredible in view of the fact that the patient had never had gall-stone colic, had never had dysentery, and at the time of the examination there was no sign of jaundice. Acceding to the advice of the surgeon an exploration of the liver and gall-bladder was performed on January 12, 1918.

Careful examination of the upper and under sides of the right and left lobes of the liver, and exploration with a long needle in several directions failed to reveal an abscess or pus. The surgeon carefully examined both kidneys, the spleen, and all of the other abdominal viscera, with negative findings. The gall-bladder was opened and showed normal walls, normal bile, no stones, and no signs of infection in the bladder or in the bile-ducts. A drainage-tube was inserted in the gall-bladder and the wound closed. The patient made the usual surgical convalescence, without any influence upon the temperature. During the surgeon's observation of the patient he was, without my knowledge, given daily for eight days 30 grains of quinin intramuscularly, without any result other than a painful abscess in the gluteal muscle.

February 10th patient was seen in consultation with a genito-

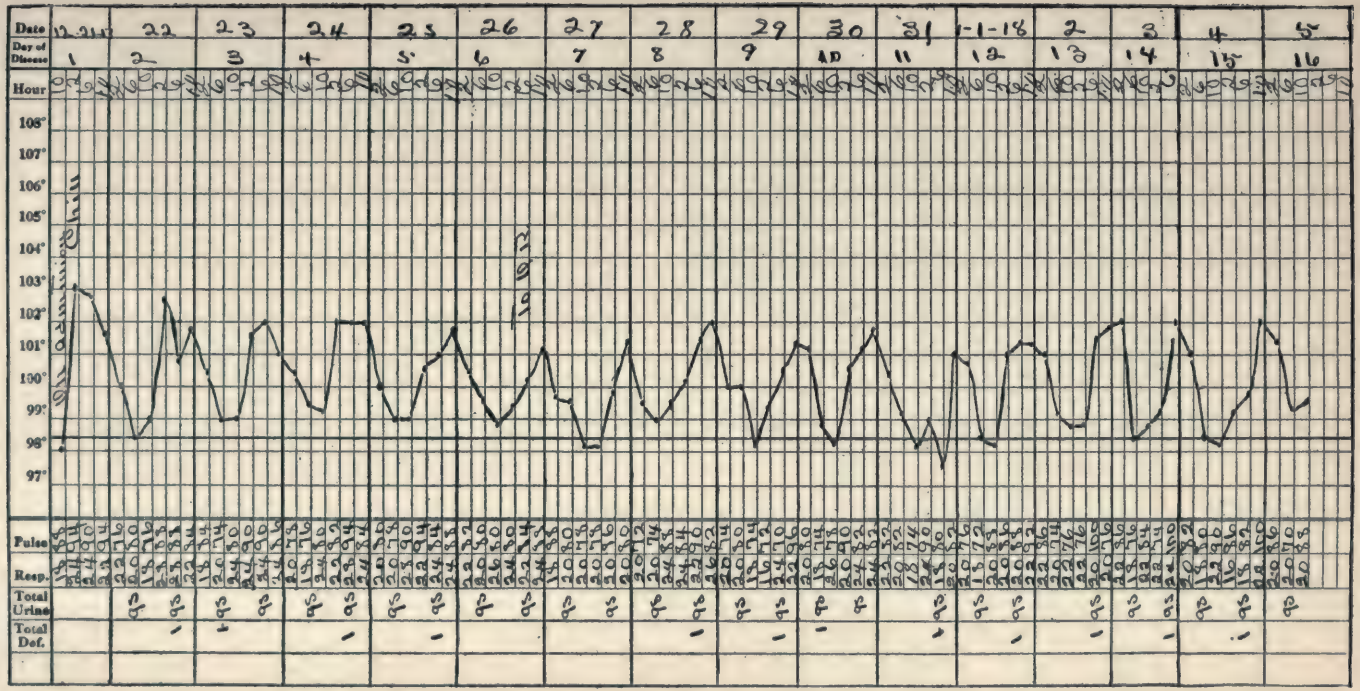

Fig. 267.—Temperature chart of Case III for one week.

urinary surgeon. A blood-culture was advised. This was made and incubated for seventy-two hours, but showed no growth at all. A cystoscopy was performed. The bladder was found negative. No stones. Both ureters patulous. Urine obtained by catheter from both kidneys collected in sterile tubes and inoculated upon suitable media, incubated for seventy-two hours, showed no growth.

During the entire course of his illness the patient frequently called attention to the fact that years ago he undoubtedly had syphilis, and repeatedly asked if it could be possible that the old trouble was recurring. As a result of these inquiries two Wassermann tests were made prior to November. Since that time several Wassermann tests according to the old antisheep hemolytic system with beef heart antigen, were personally made by me, each time without even a doubtful reaction.

In the face of these repeated negative Wassermann reactions it was only reasonable to assume that syphilis was not a causative factor, especially as the patient did not show a sign of the disease in his skin, joints, or reflexes.

The patient was fast becoming very restless over our utter inability to control the fever, and in sheer desperation before advising a change of climate (the last resort) I suggested that he allow me to give him an intravenous dose of salvarsan, with the idea of making a provocative Wassermann test, if not directly benefiting him. On February 12th, diarsenol, 0.4 gm. in 250 c.c. of saline, was given intravenously. In forty-eight hours the blood was drawn for a Wassermann. Careful examination showed a doubtful reaction.

In the meantime the patient's temperature had become normal, strength and appetite returned, and there was such a marked and noticeable improvement that he urged me to repeat the dose as soon as it was safe. Since that time at weekly intervals the patient has had four doses of diarsenol, his temperature has been normal, he has gained a great deal in strength, and has gained in weight 15 to 20 pounds.

I think there cannot be any doubt of the part that syphilis played in the production of fever in these two cases. Case I

showed a 4 plus Wassermann reaction, presenting a remittent type of temperature, simulating an atypical typhoid fever, not responding to the usual laboratory tests for typhoid fever, showing no effort at all to run a normal course, as a typhoid fever, and only responding, and then rapidly, to antisyphilitic treatment.

In Case II the evidence is just as complete. While the Wassermann reaction can usually be relied upon when it is positive, it is known by every laboratory man that it means nothing when it is negative, and no one would dare say that an individual did not have syphilis because one or even several Wassermann tests were negative.

The irregularity of fever in the case, and the fact that during a few months in 1917 there was a remission, can be explained upon the theory that gummata or foci in the liver or other abdominal viscera had healed during the time, and others had appeared and broken down later on and had produced the temperature.

Cases of this character, with the successive healing and recurrences of gummata with irregular temperature, have been reported by many observers. Especial attention has been called to this characteristic of the disease by Billings.

CLINIC OF DR. C. C. BASS

CHARITY HOSPITAL, NEW ORLEANS

MALARIA

Three Types Represented by Cases Presenting Various Features, and the Proper Treatment of Each Type; Diagnosis, Prognosis, and Treatment. Methods of Administering Quinin.

GENTLEMEN: We have for your attention today three cases presenting different features of malaria and its treatment.

The first case is an emergency case and must have our immediate attention. The patient was brought in unconscious by the ambulance from the parish prison about twenty-five minutes ago. The only history we have as to the present illness is that the patient was picked up on the street by the police patrol about three hours ago, unconscious and supposed to be drunk. After being in the police station a couple of hours his temperature was taken and found to be 104° F. The ambulance was then called and he was sent to the hospital. This suggests the importance of promptly taking the temperature of all unconscious supposedly drunk persons brought to the police station.

The patient, as you see, is a white male about thirty-five years of age and apparently a foreigner, probably an Italian. He has several tattoo marks on his arms and chest which suggest that he may be a sailor, and therefore may have recently been journeying in countries outside of the United States. He is in a state of coma from which he is not roused to consciousness by shaking, calling, or sharp pain caused by pulling the hair. The pupils react slowly to light and the patellar reflexes are below normal, but present.

A hurried physical examination does not reveal anything abnormal in the thorax. The liver is enlarged about two fingerbreadths below the costal margin. The spleen is enlarged about four fingerbreadths below the costal margin and is very hard.

There is no tympanites. There is no apparent edema of body or extremities.

We should think of nephritis or diabetes in the presence of coma of unknown cause; and this calls for an examination of the urine. A specimen was promptly obtained by catheterization, and the report is that it contains a trace of albumin, but no casts. There is no sugar present. This examination eliminates nephritis and diabetes as possible causes of the present condition.

The patient's temperature by rectum is 105.2° F. As soon as he was brought in the intern, Dr. ———, very properly collected a blood specimen for microscopic examination. He has already reported that there are large numbers of estivo-autumnal plasmodia present. He says that apparently about one-third of all the erythrocytes contain parasites. There is no apparent leukocytosis, but no count has been made.

The diagnosis of comatose malaria of the most severe form is now very plain and the patient's life is in great danger. Whether he recovers or not depends very largely upon getting a dose of quinin into his blood-stream with the least possible delay. We will therefore proceed to give him a dose of quinin intravenously at once. After doing that we will discuss the case further.

We have a 20-c.c. all-glass syringe with a No. 24 needle, direct connection, all sterile. We drop two 5-grain tablets of quinin bimuriate into the barrel and put the piston back in place. We now draw up into the syringe a few cubic centimeters of sterile water and with a little shaking of the syringe it is quickly dissolved. Next we expel a little air that was present and draw up more water until the syringe contains about 20 c.c. It is ready for administration.

While I was talking to you and preparing the quinin solution my assistant has, with the best of intention, very awkwardly constricted and prepared the arm. Note that he tied a bandage around the arm to distend the vein. Please note here on the other arm how perfectly satisfactorily the vein can be distended by gripping with one hand above the elbow. The pressure is under better control; it can be released more easily and is more satisfactory in every way.

Any prominent large vein may be used, but generally the median basilic is the best. The skin over the site of the proposed puncture is sterilized by applying tincture of iodin to an area about the size of a dime, and not 4 or 5 inches square, as was done on the other arm.

Now I disconnect the needle from the syringe and stick it well into the vein. See how I hold the skin taut with a finger just below where I stick the needle in. The blood flows freely through the needle, showing that it is in proper place. I connect the syringe with the needle and my assistant releases his grip on the arm. The solution is forced slowly into the vein. It flows fast enough if it is al lin in two or three minutes. Then the needle is withdrawn and pressure is quickly made over the puncture for a minute or two. The iodin is removed from the skin with alcohol. No dressing is needed for so small a wound. It is better without it.

In view of the patient's condition he will be returned to the ward at once. He will be in Ward 19, and those of you who have the opportunity may see him there later and watch the progress of the case.

In this case the hope of saving the patient's life depended upon getting sufficient quinin into his blood-stream to kill the malaria parasites present there. The patient being unconscious, it would have been difficult at least to get him to swallow quinin in any form, and if swallowed it would be very doubtful when it would reach the blood-stream. When taken into a normal stomach quinin appears in the urine in about two hours, and the maximum amount is eliminated about the eighteenth hour. For this patient to have to wait several hours for quinin might prove fatal. On the other hand, when we introduced the quinin directly into the blood-stream its effect upon the parasites was certain and began in full force at once.

Experiments show that when quinin is given intramuscularly the rate of absorption and elimination is about the same as when it is given by mouth, provided it is properly diluted. If, on the other hand, the solution given is too concentrated or if it is put into the subcutaneous cellular tissue the absorption is much

slower. In instances where it produces necrosis of tissue and abscess (and these instances occur quite frequently) the quinin is never absorbed. Even where severe inflammation of the tissues occurs (and this is very frequent) the quinin only reaches the blood-stream slowly over a period of several days.

Thus you see that it would be several hours or even several days before quinin given intramuscularly would reach the blood-stream, and the patient might die of malaria with enough quinin in his tissues to save him if it had been put in his blood. When we give it intravenously, on the other hand, all is accomplished that may be accomplished by quinin.

It must not be expected that quinin given intravenously will save every case of comatose malaria, for in many instances the damage already done will be destructive of life in spite of the treatment. Again, it must be understood that quinin only kills those parasites that are in the circulating blood, but it does not affect those lodged in the capillaries as long as they remain there.

The life cycle of the estivo-autumnal malaria parasite is thirty-six to forty-eight hours. During the first eight to twelve hours of this period the parasite is small and is to be found in the circulating blood. After this time, when the parasite gets larger, past the ring stage, it can no longer pass through the capillaries, but lodges in them, where it remains during the balance of the life cycle. Capillary loops are obstructed by the parasites lodged in them and, of course, no blood flows through such obstructed capillaries. Whenever sufficient of the capillaries of the brain are obstructed in this way there is much anemia of the brain and the patient becomes comatose. We call it comatose malaria. It would not matter how much quinin there was in the circulating blood, none of it would reach those parasites in these closed capillaries. After a parasite segments in a capillary the young parasites are swept out into the blood-stream. If quinin is present in the blood in sufficient concentration, they are killed. Young parasites are continuously appearing in the blood-stream, especially in such severe infections as in this case. It therefore is desirable to have quinin in the blood-stream continuously to kill them as they appear.

Whenever a dose of quinin is given by mouth or intramuscularly it reaches the blood-stream slowly, but it is also slowly eliminated. On the other hand, when given intravenously it is much more rapidly eliminated, and in a few hours following a given dose the blood would contain only a small amount of quinin. It therefore is necessary to repeat the quinin every few hours, and in urgent cases as often as every two or three hours. In this case we will give another dose of 7½ grains in about two hours. After that time he will be given a dose not exceeding 7½ grains about every six hours until he is able to take quinin by mouth. If he recovers, it is most likely he will be able to take it in this way within twenty-four hours from now. Just as soon as he can take quinin by mouth the intravenous quinin will be stopped. Whenever quinin has been given intravenously quinin by mouth is frequently neglected. This should never be done.

Please let me call your attention to the doses I employ. Here we have perhaps the most urgent condition we will ever see in malaria, and I have employed what I consider the largest dose ever demanded or justified. Ten grains of quinin will kill just as many of the parasites in the circulating blood as any larger dose will, and there is no danger of doing the patient great harm. Much larger doses, even 20 or 30 grains, are dangerous, and in some instances may be destructive of life. Of course, with a patient in such extreme condition as this one, if he should die within a few hours as a result of the toxic effect of quinin, we would not be likely to recognize the true cause of death. In a number of instances in my experience comatose malaria cases have been given larger and larger doses of quinin intravenously until they finally died of quinin-poisoning. At the time of death there would be few if any parasites in the circulating blood and the autopsy would fail to show sufficient malaria parasites in the tissues to explain the death. I would hesitate to say what percentage of all the deaths in comatose malaria in my experience I think were due to the toxic effect of excessive doses of quinin, given intravenously especially.

As soon as this patient can be given medicine by mouth the specific treatment from that time on will be the same as it would

be for any other case of severe malaria. That would be 10 grains of ordinary sulphate of quinin three times each day for a period of three or four days, and then a dose of 10 grains every night just before retiring for a period of eight weeks. At the end of this period of systematic treatment the patient should be free of malaria parasites and would not be in danger of suffering a relapse.

NOTE.—[The subsequent history in this case is that the patient improved somewhat more rapidly than was expected when he was first seen in the clinic. Within three hours the coma had almost entirely cleared up. The patient talked fairly intelligently at times, but seemed more or less dazed, and would quickly drop back to sleep when let alone. The condition finally cleared up in about twenty-four hours. The temperature was recorded normal just forty hours from the time he was given the first dose of quinin intravenously.

Three hours after the dose of quinin was given in the clinic he was given another dose of 7½ grains intravenously, and about one hour after that he took 10 grains of quinin sulphate by mouth. He was not given any more quinin intravenously, but took 10 grains every eight hours for four days, and after that 10 grains each day. His improvement was rapid and uneventful. On the ninth day after admission he left the hospital, contrary to our advice, to join his ship which was leaving port. At that time he was still quite anemic, hemoglobin 55 per cent., and his spleen still enlarged, though smaller than upon admission.]

In all cases of acute malaria, a preliminary purgative of one kind or another is beneficial and should be administered. There is much difference of opinion as to whether a simple purgative, such as the salines, is best or whether a dose of calomel followed by a simple purgative is best. I am not sure that the calomel has any special advantage, but confess that I prefer and use it in all acutely ill malaria cases. One thing I am sure of is that whatever purgative may be given, it is not proper to wait for its action before beginning the quinin. The purgative may be helpful, but quinin (and other cinchona alkaloids) is the only specific remedy known for malaria. Nothing should stand in the way of starting

its use as soon as the diagnosis of malaria has been made. The time to start quinin in any case of malaria is when the diagnosis is made.

Only recently an instance came to my knowledge where waiting for the action of a purgative resulted in the death of a patient who should have been saved. A child six years of age had a very severe chill and high fever. This was the third chill and fever coming at the same time of day on each of three successive days. A physician was called and he promptly made a definite diagnosis of malaria and recognized the severity of the case. He prescribed some calomel to be taken that night to be followed by a saline the next morning, and advised that quinin be started after the purgatives acted off. It happened that the purgatives did not act during the next day after his visit, and therefore the quinin was not given.

In the afternoon another very severe chill occurred, followed by convulsions and later coma. The physician was again called and then started giving quinin hypodermically. During the following six hours he gave this six-year-old child 60 grains of quinin dihydrochlorid hypodermically or intramuscularly. This would correspond to about 200 grains for an adult. The child died the next day, never having come out of the coma. It is impossible to know whether malaria or the quinin was the cause of death, but it is reasonably certain that if proper quinin treatment had been started at once upon the first visit the malaria would not have caused death nor would there have been any excuse to administer such large doses of quinin. That amount of quinin, if absorbed, would be likely to cause death. If it was not absorbed, as was probably the case, the patient died with many times enough quinin in his tissues to have saved him if it had been given earlier and properly. Do not wait for the action of an antipyretic or a purgative before starting proper quinin treatment in malaria. Begin the quinin at once in all cases.

The next case for our consideration is reported to be a case of malaria in which quinin given by mouth and also hypodermically has failed to relieve the clinical symptoms of the disease. The

patient was brought to the hospital by Dr. ——— from Slidell, Louisiana, arriving last night. The doctor has kindly waited over and has given us a complete history of the case.

The patient, Mr. E. A., is thirty-four years of age, and is a ship carpenter. He claims not to have been sick in any way in twenty-one years until the present time. He lived in Cleveland, Ohio, all his life until he came to Slidell, La., about eight months ago. He drinks beer occasionally.

About one month ago he had a chill followed by fever. The physician called in that evening decided it was malaria and gave him some calomel and quinin. He took the quinin for about a week according to his physician's instructions and has remained well until the present attack, which began just three weeks after the previous attack.

Eight days ago, while working in the shipyard, he was taken with a chill and vomited a few times. This was promptly followed by severe headache, backache, and considerable fever, which he thought was the same trouble that he previously had. Instead of calling a physician that day he decided to take some "Black Draught" with which his roommate assured him he had stopped the malaria on himself many times. He did not return to work the next day, though he felt fairly well, but did return the following day. At about the same time in the afternoon he had another attack of chill followed by fever, and this time called in the same physician.

The doctor felt confident that this was a relapse of the malaria he formerly had, but decided that before putting the patient on quinin again he would have the diagnosis confirmed by microscopic examination of the blood.

He sent a blood specimen to the State Board of Health Laboratory and received a report the next afternoon that estivo-autumnal malaria plasmodia were present, both rings and crescents. The patient was started taking quinin that night, 5 grains every six hours. The next day he had another chill and fever at about the same time of day the previous paroxysms began, and quite as severe as they were.

Disappointed at the failure of the quinin given to prevent the

chill, the doctor decided to try giving it hypodermically. A hypodermic of 10 grains of quinin bimuriate was given that night following the chill, and a similar dose night and morning for three successive days. Both the physician and patient were delighted with what were considered good results from the hypodermic administration of quinin, and no doubt they were impressed with the apparent superiority of this method of administration over the older method of administration by mouth. On the fourth day, however, the patient felt dull, languid, had a headache, and about noon had a slight chill. His temperature was 102.2° F. when seen by his physician at 2 o'clock. It was then decided to bring him to the hospital and learn what explanation we might offer for the failure in treatment, and especially what method of treatment would be advised. Dr. ——— is present and the patient is before us now.

The patient appears well nourished and not very sick. You will note, however, the flushed cheeks and eyes rather injected. You have noticed, no doubt, that since we have had him in the amphitheater he has been rather restless, turning on his cot frequently, as if trying to get comfortable. This may be due to nervous temperament and unimportant, or, what is more likely, it may be due to his fever, which is 101.6° F., and to the condition causing it.

There is nothing noteworthy recognized about the head and neck except the flushed cheeks and injected eyes. This is no more marked, however, than may be seen in fever due to a variety of things.

Nothing abnormal in the heart and lungs can be made out. Pulse 102, regular, rather full. Respiration 24 per minute.

The liver cannot be palpated and no liver dulness can be made out below the costal border.

Since malaria is especially to be considered, we should give special attention to the spleen. There is almost always some enlargement of the spleen in cases of malaria of more than a few days' duration. Yes, this one is distinctly palpable when the patient forces it down with the diaphragm by deep inspiration. With the patient lying on his back and his knees drawn up to

relax the abdominal muscles I can palpate best with my right hand resting on his abdomen and the tips of my fingers directed up nearly to the costal border. With my left hand back of the spleen region I lift it forward. This tends to shove forward and render an enlarged spleen more easily palpated. Now as the patient takes a deep breath the edge of the spleen strikes against my finger-tips and is readily recognized. Let us see if we cannot demonstrate it so you can see from your seats. When the patient takes a deep breath and forces the spleen against my fingers I press upward against it somewhat beneath the edge. Then I slightly relax the pressure and allow the edge of the spleen to slip suddenly beneath my finger-tips. It is distinctly felt and you see the fingers suddenly slip over it.

The abdomen is rather flat, the patient having been given a saline last night and an enema this morning. Nothing abnormal is made out. There is no tenderness.

The patient complained of my hurting his arm a moment ago, and now upon examination we find what should have been observed or found out sooner. There is an area of purplish redness about 4 inches in diameter around the insertion of the deltoid, which we are informed is the site of the first hypodermic injection of quinin given five days ago. It is painful and when compared with the other arm is somewhat swollen. Upon deep pressure the center especially feels boggy. Here we have a probable explanation for the fever he now has—inflammation and probably necrosis of tissue resulting from the hypodermic injection of quinin.

The blood was examined early this morning for malaria plasmodia and none found. Another examination was made about 10 o'clock, with the same result as to malaria. There were 15,400 leukocytes per cubic millimeter and the differential leukocyte count showed small mononuclears 16 per cent., large mononuclears 2 per cent., neutrophils 82 per cent., eosinophils none, basophils none. A moderate leukocytosis and a definite "septic factor" is present. We are justified in concluding that the present condition is due to the effect of a hypodermic of quinin and not to malaria. If malaria was the cause of the present fever

we should be able to find malaria plasmodia in the blood and there would be no leukocytosis. Simple malaria never causes leukocytosis or the "septic factor" in the differential leukocyte count.

We should emphasize also that this is not a case of malaria in which quinin has failed to control the clinical symptoms of malaria, as it was supposed to be.

Very likely the quinin that caused so much local damage was injected rather superficially into the subcutaneous cellular tissue and not deeply into the muscular tissue. It is much less likely to produce necrosis and abscess when put into the muscular tissue. The solution used was also most likely very concentrated. The more dilute the solution, the less likely to do damage. I do not think quinin should ever be given hypodermically or intramuscularly, but if there ever occurs an instance when quinin should be so given it should be diluted at least ten times. Ten grains of quinin dihydrochlorid should be dissolved in no less than 6 c.c. or $1\frac{1}{2}$ drams of water.

As for the treatment in this particular case, we have a condition likely to require surgical attention in a patient also known to have malaria. It will be impossible to say at the present time whether the damaged tissue will break down and abscess or not, but most likely it will. The damage is done by the chemical action of the quinin on the tissue causing inflammation or necrosis, and not to infection, as is often supposed. Unless there is considerable improvement in both the general and local condition shortly, incision, permitting drainage, will be indicated.

So far as the malaria is concerned, the patient should be treated as any other patient who had just been relieved of the clinical symptoms of malaria would be treated. That treatment is 10 grains of quinin sulphate in capsules every night for a period of eight weeks without intermission. He will then be free of malaria parasites and will not relapse again.

The third patient was kindly sent in for our clinic from the Outpatient Department. The diagnosis made is malaria relapse; intermittent malaria.

Mr. J. C. McL., age forty-two, a resident of New Orleans for the past twelve years. He has been a bill clerk in a wholesale grocery store for the past seven years.

His family history has no bearing upon the present trouble except that two younger brothers were having chills and fever at the time he paid a visit of a week to his family in Mississippi, in June, 1915.

The only sickness he has had during the past several years has been repeated attacks of chills and fever during the past three years. He now comes to the clinic for one of these spells of chills and fever of about one week's duration.

He visited his old home near Hattiesburg, Mississippi, in June, 1915. At that time two brothers were having chills and fever. In about ten days after returning to New Orleans the patient had a chill one morning about 11 o'clock, followed by headache and fever, which passed off during the night. He felt pretty well the next day, but on the following day another chill came on just forty-eight hours from the onset of the previous one. He treated himself with chill tonic, which broke up the chills after the third one had occurred.

In a few weeks he had another attack, having a few chills, each followed by a few hours of fever of the same type as before. This time he consulted a physician, who gave him a prescription and told him to take some quinin.

Since that time he has had two or more attacks of one or more chills and fever each every year. He has been treated by three different doctors during the time. They always stopped the chills, but they would come back. Patient says he has taken a "bushel of quinin" and "one doctor put it into" him with a hypodermic needle. This was in the fall of 1917, and he thought he was cured, but now he is disappointed that it "has come back on" him again. He is quite confident there is no use for him to try quinin any further.

During the present illness the patient has had four chills followed by fever, each occurring about 2 P. M. every other day, the last one occurring yesterday. The chills last fifteen minutes to half an hour and the fever not more than six or eight hours.

There is much headache and backache during the attack. Patient says he "burns up with fever." Also that the present attacks are just like those he has been having for three years.

Upon physical examination nothing abnormal is found. There does not seem to be any enlargement of the spleen. The patient, as you see, does not appear to be sick. He looks fairly well and there is no anemia apparent.

A blood examination made this morning shows tertian malaria plasmodia present and a few stippled erythrocytes. There is no leukocytosis. The differential leukocyte count is within the normal limits. Hemoglobin by Tallqvist's scale 80 per cent.

The diagnosis is tertian malaria. In view of the history and in view of the fact that he has not been out of New Orleans, where there is practically no transmission of malaria, since 1915, it is reasonably certain that this is a relapse produced by the original infection he got three years ago.

Careful inquiry from him indicates that from first to last he has taken quinin during more than three months of the three years since the infection occurred. Most of this was taken in very variable doses, however, and for a few days at a time. In one instance he says a doctor gave him two capsules (a very indefinite quantity) of quinin every day for three weeks. He has not, therefore, taken quinin in such a way as to be at all certain to get rid of the infection, though, as he says, it always relieved the symptoms for a while.

Our advice is that he take 10 grains of quinin sulphate in capsules three times each day for three successive days. Usually if the quinin is started twenty-four hours or longer before the next chill is due it will be missed. If only started a shorter time before the next chill is due the chill will often come on, no matter how large the dose of quinin. After he takes 30 grains of quinin a day for three days, then he should take 10 grains every day (preferably every night before retiring) for a period of eight weeks without intermission. At the end of this treatment he will be free from infection and will not relapse again.

CONTRIBUTION BY DR. LAWRENCE T. ROYSTER

NORFOLK, VA.

THE CARE OF THE PREMATURE INFANT[1]

IN the care of the premature infant we are confronted with one of the most difficult and serious problems in medicine; there is no problem, however, which offers a more gratifying reward of success when painstaking, intelligent management is instituted. Attention to details is essential to the success of all medical and surgical cases; even the aseptic technic of the operating room is of no more importance than attention to the minutest detail in handling a premature child. Under the best conditions the mortality is exceedingly high, but many children can be saved if given proper attention. The life of the child depends largely on the degree of prematurity and state of development. For example, a child may be born at seven months weighing more than another born at eight months. But a six or six and a half months' fetus weighing 3 pounds or less has, under the best conditions, an exceedingly poor chance. Cesarean section in obstetric emergencies has vastly increased the chance of life of the premature from these causes over any form of accouchement forcé.

The main indications in handling premature infants are "the maintaining of normal heat, the nourishment of the infant, and the prevention of infection," therefore, the subject will be discussed along these lines.

All newborn infants have the heat-regulating center poorly developed. Even with normal infants it is unwise to expose them to sudden changes of temperature. It must be remembered that at birth the infant passes abruptly from an environment the temperature of which is 100 degrees to one 15 to 30 degrees lower.

[1] Read by invitation before the George Washington Medical Society, Washington, D. C., April 16, 1918.

This is naturally a shock—one often sufficient to determine the matter of life or death of a very weak, premature infant. Hence, every effort should be made to overcome this shock where possible. Only too often, not only in house practice, but even in some of our best hospitals, no provision whatever is made for the care of the premature. The mother's condition may be so grave that her welfare alone is considered by both physician and nurse, and the infant is neglected sometimes for hours. This should not be the case. Some capable person should be delegated with the entire care of the newborn patient, and, preferably, if the case is to be turned over to a pediatrician he should be present so as to assume the care of the infant from the moment of its birth. When a premature birth is anticipated, whether normal or operative, a warm blanket covered by a warm sterile sheet or towel should be kept at hand in which to immediately wrap the baby. This procedure alone will save many of these little ones.

If the infant is born asphyxiated it has a serious handicap, for the premature cannot well stand the usual methods of resuscitation and very little slapping or waving should be permitted; under no circumstances should the child be submerged in cold water. All necessary resuscitation should take place in a room sufficiently heated to prevent material radiation. The maintaining of body temperature should then be our first care, and this can be done always within 1 degree and often within the limits of $\frac{3}{8}$ degree. Because of the poorly developed heat-regulating center already referred to the infant responds very rapidly to its environment. It must be understood that the handling of the infant must be done with surgically clean hands on the part of the attendant.

The infant should not be bathed at all, but should, on alternate days, be oiled with warm sweet oil. The question of incubators is a mooted one. Outside of well-regulated hospitals with nurses trained in the handling of premature infants and the management of incubators they are not successful. Personally, I do not employ them; instead I have with good success made use of the so-called premature infant's gown or jacket (Figs. 268 and 269). This is made of non-absorbent cotton batting, about $\frac{1}{2}$ inch

Fig. 268.—Premature infant's jacket.

Fig. 269.—Jacket applied.

thick and quilted between layers of gauze with a hood attached which covers the head. This is made as a one-piece garment. No clothing whatever is employed. As soon as the infant is delivered

it is well oiled and placed immediately in the jacket, which is pinned up the front with safety-pins in a similar manner to a surgical binder. The bottom is then turned up and pinned. No napkin is used, but in its stead a small pad, 4 or 5 inches square, made of quilted cotton and gauze similar to the jacket, except that for the pads absorbent cotton should be used. These pads are changed whenever soiled. A hamper clothes basket or bassinet is employed as a receptacle. A pillow is placed in the bottom and pressed down in the middle, the baby now enclosed in the jacket is placed therein and covered with several folds of blanket and hot-water bottles or bags placed so as to surround the infant.

The infant is not removed from the basket for any purpose save its oiling and weighing every other day, except when strong enough to nurse, and then it is put to the breast in the jacket. The body temperature should be maintained between 98° and 99° F., which can be done readily by means of hot-water bags or bottles or by an electric pad, which may be attached to any socket. I am told that these pads require close watching, since they sometimes get out of order and may cause trouble. The infant's temperature should be taken at four-hour intervals per rectum; for this purpose the jacket is opened at the bottom and the nurse's hand run up through the jacket to the baby's rectum.

In order to aid us in maintaining the temperature another thermometer, such as an ordinary bath thermometer or one enclosed in a glass tube, may be placed between the infant's jacket and its covering blanket. So long as this is kept at 90° F. we are safe in assuming that the baby's temperature is within the desired limits. On alternate days the infant is transferred in its basket to a room such as a bath-room which has been previously heated to as near 90° F. as possible. Everything being in readiness, the jacket is removed, the baby is quickly weighed and oiled with warm oil, and again wrapped in a clean warm jacket. This whole procedure need not occupy more than two or three minutes. This method of maintaining heat is quite as successful as the use of an incubator. The infant is usually kept in the jacket until its weight is 6 pounds.

The second indication, that of nourishment, presents the greatest difficulty. Two facts must be constantly borne in mind. First, that the infant is born at a time when its powers of digestion are not sufficiently developed to take the food which is usually supplied to a full-term baby, and second, its strength to nurse is so slight that breast or bottle feeding is quite out of the question.

Breast milk is, of course, desirable; in fact, in the very delicate is absolutely essential to success. Generally the mother's own milk does not appear promptly in the very premature cases, and recourse must be had to the milk of some other woman. In the meantime a strong, lusty baby may be put regularly to her breast for the purpose of stimulation. As a rule, a premature infant cannot digest whole human milk, so in the beginning even this must be diluted one-half and in some instances one-fourth with 5 per cent. milk-sugar solution. This is gradually increased in strength until human milk of full strength is administered. As the child develops, if it becomes necessary to give up human milk we may safely give modifications of cows' milk. In some instances it may be impossible to secure human milk and it may be necessary to use cows' milk from the beginning. A number of my most successful efforts have been under such circumstances. When such a procedure is necessary the following outline is suggested:

The usual initial loss in weight of newborn infants may be in part physiologic, though sometimes it is no doubt due to the fact that the mother's milk does not appear until the third day. Dr. Fritz Talbot has successfully demonstrated that this initial loss may be prevented in large measure by giving a 5 per cent. solution of milk-sugar from birth. Premature infants can ill afford any initial loss, however small, hence I have adopted the routine of administering a solution of milk-sugar at once. This is replaced by some other form of food as soon as possible. I have found whey of inestimable value in these cases. This may be made from whole or skimmed milk, according to whether we think the infant can take any fat at all or not. If made from skimmed milk we have a formula which is approximately F0.

S4.50. P90 (whey protein). This is usually well borne and will serve to prevent any loss, and even in most instances furnishes sufficient food to cause a considerable and steady gain in weight. However, we cannot expect a gain for a very long time on such a mixture, and so when the child appears to have a fair start we gradually change to a formula of cows' milk. This change must be made at first by adding skimmed milk to the whey, thus giving the so-called "split protein," *i. e.*, whey protein and casein. From this we begin to skim off less and less cream from the milk used to make the whey, until we have whey made from whole milk, which gives a fat percentage of 0.90. When this stage has been reached we change to a formula of cows' milk of approximately F.75. S.5. P1. After this the conduct of the case may safely be pursued along regular lines of increase.

The interval of feeding and the quantity taken at each feeding depend entirely on the infant, as is the case in feeding a normal well infant. A small premature rarely takes more than ½ ounce at a feeding, and many times 2 drams may be the limit. The best interval for quite a while is two hours.

The manner of administration varies with the exigencies of the case. A strong and but slightly premature infant will take the breast or bottle readily; the further we get away from full term, however, the more difficult the problem becomes. The Breck feeder is very useful not only as a feeder but also in teaching the infant how to nurse. More frequently we have to begin with a medicine-dropper, and quite often it becomes necessary to resort to gavage where the infant is too weak to nurse. To keep the baby alive it is quite obvious that we must supply the nourishment in whatever manner necessary. Gavage is not difficult. A small rubber catheter and a glass funnel are all that is needed. The tube is passed either through the nose or directly into the esophagus through the mouth. During this procedure the infant does not have to be moved from the basket. It is very important to keep the food warm while waiting to use it, and the best way to do this is to set the container in a bowl of warm water.

The third indication—prevention of infection—is exceedingly important. The avenues of infection most usual in these cases

are the mouth, the lungs, and the umbilicus. The mouth should be kept as clean as possible. It must be remembered that a baby's mouth is sterile, and if infection occurs it does so from without. Sterile water should be used once each day. Absorbent cotton and not gauze should be wrapped about the little finger, dipped in the sterile water, and every part of the mucous membrane of the infant's mouth cleansed thoroughly, but very gently. The habit of washing out a baby's mouth at each feeding is pernicious and should be abandoned. The greatest care should be exercised in keeping the nipples clean. The part of the nipple which goes into the mouth should not be touched after boiling. I do not keep nipples in solution at all. After a thorough cleansing and boiling they are kept dry in a preserve jar or other covered glass receptacle. At the slightest indication of coryza on the part of either the attendant or the nursing mother masks should be used to prevent the infant's acquiring the coryza and possibly a subsequent pneumonia.

The incidence of pneumonia should be scrupulously guarded against, since this disease causes a very large number of deaths among premature infants. Although it is necessary to maintain body temperature as already outlined, the infant must not be kept in a close, stuffy room. The room in which the baby lives should not exceed 72° F. at any time, and a free flow of fresh air should be assured. In very cold weather in steam-heated rooms the heat should be kept in the radiators, but the windows raised enough to secure free circulation. Whether radiators or stoves are used, moist air must be assured by a pan of water constantly kept near or at the source of heat.

Cool fresh air does not cause pneumonia, but rather prevents it. Hot, stuffy air is one of the best means of producing it.

Prevention of infection of the cord is easiest accomplished by letting it absolutely alone when the proper initial dressing has been applied until it has come off and has healed.

CONTRIBUTION BY DR. J. ROSS SNYDER

BIRMINGHAM, ALABAMA

A STUDY OF 10 PELLAGRINS IN TWO FAMILIES LIVING IN THE SAME NEIGHBORHOOD[1]

ON the morning of June 20, 1917, a mother carrying a sick child in arms applied at the Children's Hospital for the services of a physician. There is no resident physician at this institution, but the mother was urged to await the arrival of the attending physician. Although the mother believed her child to be dying, she said she would be compelled to go back home because she had left there other children unattended. She refused the offer to admit the child to the hospital. Soon after her departure I was informed of the above facts. Obtaining the address, which the admitting nurse had fortunately secured, I investigated the case. Some interesting findings were made:

The Johnson family consists of father and mother and five children. The father is thirty-three years of age. The mother is twenty-nine years of age. The family has been living at the present location since September, 1916. Previous to this time the family had lived in the country. The father is a section-hand on the railroad. His earnings are usually about $50 per month. For several weeks the father has been unable to work steadily because of bowel trouble and sore hands. There is no other source of income except the father's wage. The neighbors occasionally send in vegetables, such as cabbage, greens, and radishes. The whole family has been sickly for several weeks; the father and several of the children have loose bowels. The father and all the children have a "breaking out." The mother has no loose bowels, no breaking out, but her mouth is sore and

[1] Read before the Jefferson County Medical Society, April 29, 1918.

her stomach burns. She also has headaches and dizzy spells. The mother believes the sickness of the family is due to self-rising flour, several sacks of which were bought by her husband at a sale. The chief articles of diet during the winter months were corn-bread, potatoes, fat meat, molasses, field peas, cabbage, and coffee—on some Sundays pork chops. No milk except an occasional can of condensed milk which was bought for the twin babies, but which was never given with regularity, days often intervening between the exhaustion of the can and the ability to purchase another. Since the warm weather there has been but little change in the diet except that biscuits from the self-rising flour have taken the place of corn-bread. At the time of my visit the sickest child is lying on the mother's lap and being urged to take some underdone biscuit dipped in syrup. The other children are seated around the dinner table. The meal consists of cold boiled potatoes, biscuit, and syrup. If any animal protein is to form a part of the meal it will be furnished by the accidental ingestion of some of the numerous flies which swarm over the food and over the children's hands and faces. The child in the mother's lap is evidently very ill. The mother gives his age as three years, but except for length he looks like a marantic infant. The eyes are sunken, the lids semiclosed. The lower jaw sags—the mouth is open. The child feebly pushes away the offered food. The tongue and mouth are dry. The tongue is coated a yellowish brown, except on tip and edges, where it shows red. The teeth are sound, but the gums are swollen and red. The abdomen is scaphoid. The integument of the skin is dry, wrinkled, and loose. The child has an erythema over the entire face except for a narrow margin running parallel with the hair-line. There is also an erythema on his neck, hands, feet, and legs. There is a distinct line of demarcation between the affected and the normal skin. The erythema is bilateral and symmetric. The temperature (rectal) is 103⅘° F.; the respiration is shallow and rapid—42 per minute; the pulse is weak and rapid—160 per minute. The child's bowels move during the examination. There is considerable straining and evidence of pain. The stoolage consists of blood

and mucus—it contains no apparent fecal matter—the odor is not offensive. The mother says the child's bowels have been loose for several weeks, but that only within the last week have they contained blood. The child has had fever for about one week. For the last week the bowels move fifteen or twenty times a day. The child has vomited but once during his illness. The diagnosis is pellagra complicated by an acute ileocolitis.

An examination of the other four children shows that each has a pellagrous eruption. The twin brother of the sickest child is chubby and fat, but he has a dirty looking pigmentation on the dorsa of his feet and on the extensor surfaces of his legs. A sister, five years old, has an ulcerated sore mouth, bleeding gums, and a marked pigmentation on her feet and legs. She also has a pigmented spot on either cheek. A sister, eight years old, has an erythema with a distinct line of demarcation on the dorsa of her feet; she has also a distinct Casal's collar. The oldest girl, eleven years, has a sore tongue, red on its edges but pale and glazed elsewhere; she has an ulcer in each corner of her mouth; the backs of her hands are swollen and an erythema ends sharply 2 inches above the wrists; the eruption is also very distinctly marked on the dorsa of her feet. The father (examined June 22, 1917) has an eruption on the backs of his hands which extends 3 inches above the wrists. The skin over these areas is of a bronze hue except where the skin is fissured; these fissures, about $\frac{1}{8}$ inch wide, are numerous, and in them the surface is raw and blood oozing. The father does not use alcohol. He chews tobacco, but recently his mouth has burned and has been too sore to permit chewing without pain. His tongue is of the typical cardinal variety. The mother chews snuff, but relates that for several days past she would as lief chew a live coal as to chew snuff. Until the present summer no member of the family has been ill except that the mother has had "female trouble." The nature of this trouble is not ascertained, but is easily guessed when I am told that a country midwife presided at each of her confinements. Prior to the present summer no member of the family has had an eruption or a sunburn severe

enough to attract attention. No member of the family until the present season has had an intractable diarrhea.

It was regarded then that each member of this family was having his or her initial attack of pellagra. For this reason and for the reason that not a single member in the family escaped, it was thought that these cases deserved a more or less intensive epidemiologic study.

The Thompson-McFadden Pellagra Commission holds tenaciously to the opinion that pellagra is due to an infection, which it grants is probably low grade and not highly communicable, but is none the less an infection. Members of the Commission admit that deficient dietary is an important predisposing factor, but they insist that this factor alone cannot explain the etiology of the disease. The Commission has been impressed by the fact that new cases of pellagra develop either in the same house with or in close proximity to a pre-existing case; by the fact that endemic foci discovered during its investigations were, as a rule, centered around localities where open privies existed or where there was careless disposal of human wastes; and by the fact that in whatever of these localities there was later installed a sanitary system of sewage at once occurred a marked reduction in the number of new cases of pellagra developing.

The neighborhood in which the Johnson family lived was a poor one. The house was a two-roomed cottage in an unsanitary alley. Both rooms in the house were large and abundantly supplied with sunlight and air. A roofed porch ran the length of the northern side of the house. The house was unscreened. The alley on which the house faced was about 40 feet wide and ran south from First Avenue to the railroad tracks, a distance of 300 feet. The Johnson house was about 50 feet from the railroad tracks; the space between, as well as a considerable area in front of the house, was open except for weeds. Two other cottages of similar construction to the Johnson house were on the same side of the alley. The shortest distance between any of these cottages was 15 feet. The lots on which these cottages were built were not fenced in. A four-room cottage facing

First Avenue on a fenced-in lot 125 feet deep took up the remaining space on this side of the alley. On the opposite, the western side, of the alley were two three-room cottages facing the alley, on fenced-in lots each about 25 x 50 feet, and a double three-room cottage facing First Avenue on a fenced-in lot 125 feet deep. The two cottages adjoining the Johnson cottage were occupied by negro families. Five negro children and three negro adults were in the two families. Across the alley one cottage was vacant and one was occupied by a very old gentleman and his young daughter. No chicken, pig, or cow was kept on any of these premises. A Belgian hare was kept by the Johnson children. Two dogs and a cat were kept by the negroes. There was no crowding, but, on the other hand, plenty of air space for all the inhabitants of the alley. The inside of the negro cottages was clean and neatly kept. Both were unscreened. The negroes were careless in the disposal of waste waters and table refuse. There was no well in the neighborhood, each cottage being supplied with city water.

To the rear of each cottage was what was probably originally a sanitary privy. The construction of the privies was practically the same. It consisted of a wooden frame with one and in some instances two seat-holes. Under each hole and standing in a wooden box was a tin or galvanized iron receptacle. The rear of each privy-box had a hinged frame flap or drop intended to be kept down except at the time of removal and emptying of the receptacle in order to prevent flies, pigs, chickens, etc., from having access to its contents. The hinges on the flaps on nearly all the privies were found intact, but in several instances they were found only part way down. Covers for a number of the seat-holes in the privies inspected were found detached, and in a number of other instances they were not down in place. Many of the receptacles were found exposed and in a bad condition. This kind of a privy is attached to not only the cottages in the alley, but to all the cottages facing First Avenue for a distance of one block on either side of the alley. Their number was not counted, but was estimated to be between twenty-five and thirty. Eight of them were inspected by me, with findings as mentioned

above. The receptacles were emptied once a week. The capacity of the receptacle was about 15 gallons. Some of them were running over at the time of inspection. The privy on the Johnson lot was found to be in a worse condition than any. The rear flap was prevented from closing by a large stone intentionally or accidentally placed under one end. The receptacles were brimful and had slopped over. The seat-covers were detached and missing. The door was on one hinge. The privy inside and out was swarming with flies. Tall weeds surrounding the Johnson cottage offered conveniences which were sometimes at least preferred by the children in the family to the accommodations of the privy. To this fact my shoe at the time of my first visit bore convincing olfactory as well as ocular evidence.

So far my findings fitted well into the ideas of the Thompson-McFadden Commission with reference to the spread of pellagra. When I discovered 3 other cases of the disease, each of which gave a history of having the initial attack in the summer of 1916, living in the neighborhood, I was at first quite sure that the communicability of pellagra was going to be proved at least to the satisfaction of my own mind. These 3 cases were the McGrady children, two girls and a boy. The McGradys lived in one side of the double cottage facing First Avenue, the 125 feet lot of which formed the western side of the alley. Figure 270 shows a diagram of the alley with its privy and cottage arrangement.

Fuller investigations by me, however, weakened the evidence pointing to the communication of pellegra to the Johnsons. Aside from the members of the Johnson family, each of whom was experiencing the initial attack, and the three McGrady children, each of whom was experiencing the second attack, no other case of pellagra existed within a radius of two blocks. If the disease was communicated to the Johnsons, then it must have been communicated from the McGradys. The McGrady privy was not less than 100 feet from the Johnson house. The privy was on ground which drained away from the Johnson house. Of all the privies inspected, the McGrady one was in a sanitary condition. The rear flap was kept tightly down. The receptacle

was in good condition, was without leaks, and was carefully placed. Lime had been used inside and around the receptacle.

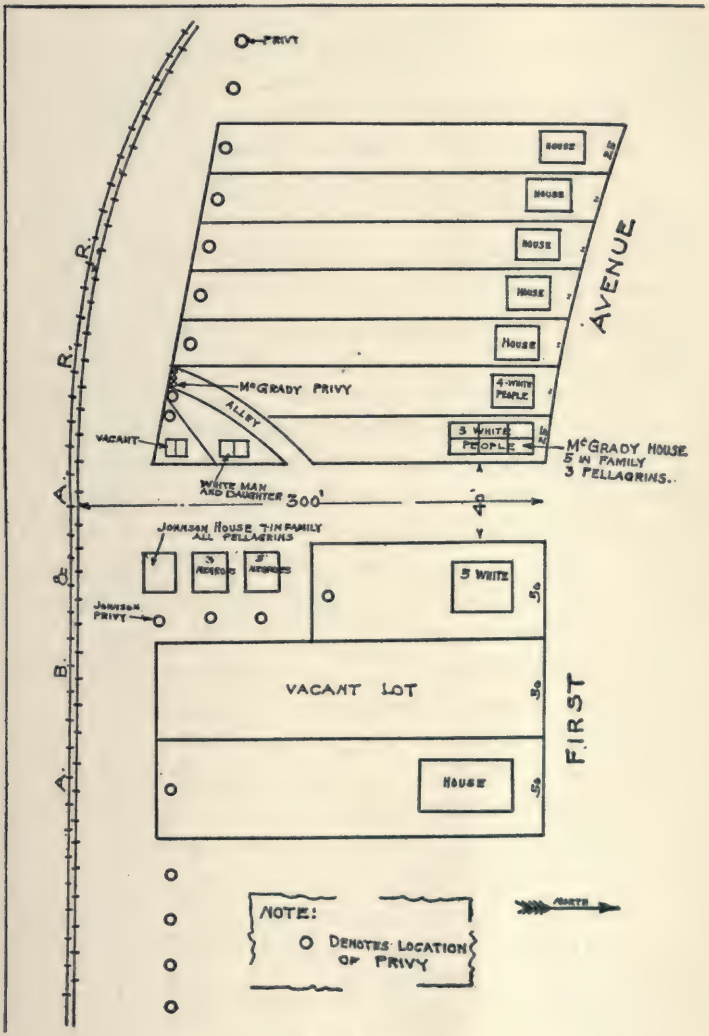

Fig. 270.

The seat-cover was down. The door was kept shut. The McGrady father was a motorman. His wife was intelligent and

was evidently a good manager. The house was screened and as clean and neat as a new pin. Father and mother and the three children constituted the household. The McGrady children were clean and neatly dressed. Although the McGrady children sometimes played with the Johnson children, there was no great intimacy, as the McGrady mother tried to discourage this. Without the offices of some insect, as a carrier, the McGrady privy did not impress me as being a probable factor in the spread of the disease to the Johnsons. There were fewer bugs and insects on the McGrady premises than anywhere else in the neighborhood. A few flies were found on the outside of the privy. One was seen on the inside. The scarcity of flies inside the closet was due to its darkness when the door was closed. In the alley itself flies of the ordinary domestic variety were numerous. Unidentified mosquitos, grasshoppers, and small yellow butterflies were also seen. Insects and bugs as a possible etiologic factor in pellagra were studied by Jennings and King for the Thompson-McFadden Commission. By convincing methods, these gentlemen were enabled to eliminate every one of the many insects which have from time to time been suggested as being in any way connected with the etiology of pellagra. For a time Jennings and King believed that the stable-fly might have some relationship to the disease. Repeated experiments conducted by them failed to sustain this opinion.

Similar though some of my findings relative to pellagra in the Johnson family were with the findings of the Thompson-McFadden Commission, I was unable to arrive at conclusions similar to those held by members on the latter body.

On the other hand, the investigations relative to the diet of the Johnson family and of the three McGrady children seemed to point very strongly to the correctness of Goldberger's conclusions. Goldberger, who believes that pellagra is in no way communicable, is of the opinion that the disease is the result of some dietary deficiency. Those of you who are unfamiliar with or rusty on the subject of dietary deficiencies are referred to the writings of Funk, Voegtlin, Vedder, etc. These men believe that in the well-balanced diet of man there are, in addition to the

commonly recognized essential elements, a certain number of specific disease-protecting elements—the so-called accessory factors or vitamins. When man lives on a diet from which any one of these vitamins is absent he will develop either beriberi or scurvy, or rickets or pellagra, depending on whichever one of the vitamins is absent. It has been definitely established that beriberi and the less commonly known disease, xerophthalmia, is each the result of living on a diet from which is absent its specific vitamin. These, then, are true deficiency diseases. So far theory alone classifies scurvy, rickets, and pellagra along with them. McCollum and his co-workers, who dispute the existence of a pellagra-protecting element or vitamin and the existence of a scurvy-protecting element or vitamin, believe that pellagra is the result of several factors, chief among which are mechanical injury to the mucosa of the intestine from continued use of inappropriate food-stuff and the resulting stimulus to bacteria ordinarily not numerous in the intestines.

There will be no attempt here to reconcile fine scientific points. As stated, the study of the diet of the Johnsons and of the McGrady children as made by me pointed to the correctness of Goldberger's conclusions. But I referred only to Goldberger's general and broader conclusions, namely, that pellagra is not communicable, but is the result of the continued use of a diet lacking in animal and vegetable proteins.

The Johnsons, as you will recall from the history, had lived in the country until September, 1916. While in the country they had no near neighbors. While in the country each member of the household had remained well. While in the country the family kept a cow and raised chickens. The mother told me that while in the country milk and eggs formed a part of almost every meal. Fried or boiled or baked chicken was served from time to time. Occasionally fresh pork was served. Occasionally fresh goat meat was served. So that though the chief meat, even while in the country, was salt pork, fresh meat was not unknown to their stomachs. The table fare after removal to the city has already been discussed. But the significance of the contrast between the food of the family while in the country and

after moving to town cannot be appreciated fully without a consideration of the findings relative to the diet of the McGrady children.

The McGradys were in no such financial distress as were the Johnsons. The McGrady income was sufficient to provide something more than the bare necessities. My offer to have milk furnished to the McGrady children out of a fund provided for by one of the daily newspapers of the city was declined. Mrs. McGrady told me that the husband and father was able and willing to amply provide food for his children. Investigation, in fact, showed that such provision was made. Investigation also revealed the fact that of the three McGrady children not one liked meat, milk, or eggs. The chief articles of diet with these children, a boy five years old, and two girls, seven and ten years of age respectively, were cereals, fruits, bread and syrup, battercakes and syrup, and green vegetables cooked with fat meat. In order to induce these children to drink milk and to eat eggs and meat it was necessary to offer rewards and prizes. It was only after several weeks of reluctant acceptance of these latter articles that a taste for them was cultivated. Therefore, though the sanitary conditions in this neighborhood were bad, though the conditions of the privies should be regarded as intolerable, though pre-existing cases of pellagra were living fairly near to the new cases, it seems to me that there was little relationship between the new and the old cases except that in both was discovered a diet deficient not in quantity but deficient in protein content.

DISCUSSION

THE PRESIDENT: Will Dr. Snyder tell us the outcome of these cases?

DR. SNYDER (continuing): Every one of the cases referred to by me in the report gained weight, had symptoms disappear, and made an apparently complete recovery in a very few weeks. Except for a dose of castor oil, administered to the sickest child, no medicine was used. The treatment was entirely dietetic and consisted in incorporating in the diet of each a larger percentage of proteins, as furnished by milk, fresh meat, and eggs.

Except in the case of the sickest child nothing was said about what should not be eaten. Corn bread, cereals, white meat, syrup, batter cakes, etc., of which they had previously partaken, were not prohibited. In fact, I remember saying to the McGrady mother that if pellagra was of dietetic origin it was caused not by what was eaten, but was caused by what was not eaten. The Johnson father, on account of his increased capacity for work, was given a promotion with an increased salary. Toward the end of the summer the family moved to another community. Up to the time of their departure they were all well. I have heard indirectly that they continue in good health. The McGrady children continue under observation. So far there is no evidence of a recurrence in any one of them.

Dr. D. L. Wilkinson: Mr. President, I do not know that I endorse in its entirety Dr. Goldberger's conclusions as to the cause of pellagra or his dietary treatment. I have seen and treated a good many cases. I have known several fairly well-to-do farmers who largely lived on milk, eggs, and chicken, and who still went on and died from pellagra. I remember in particular two brothers who were in this class, both large, healthy men, except for living in a malarial section and giving a previous history of malaria; who while they lived largely on these products and what they grew at home, still they developed pellagra and died from it in spite of Goldberger's dietary. In my experience I have seen so many cases secondary to some other trouble that at one time I almost concluded that pellagra was always secondary to some other trouble. I have perhaps treated 25 cases of pellagra and had a large percentage of them to go on and die in spite of either medicinal or dietetic treatment. I wish to thank Dr. Snyder personally for his very able and thorough paper.

Dr. W. B. Hardy: Hearing Dr. Snyder discuss the diet in pellagra reminds me of a four-year-old boy we had in the hospital recently with a second degree burn of the right side of his body.

In due time the surface was partially covered with skin-grafts, as we were unable to secure sufficient skin to cover it entirely, but, for some reason, the skin did not thrive and take hold as we had hoped it would. Two weeks later the grafts

seemed perfectly healthy, but showed no signs of spreading. At this time he was seen by Dr. Snyder, who pointed out to us definite signs of pellagra on his knees and wrists. At Dr. Snyder's suggestion in addition to his usual diet he was given milk and eggs in abundance.

After a few days it was indeed wonderful to see the change in the general condition of the child, and especially the grafts, which began to spread, and a few weeks later he was able to leave the hospital, the entire surface having healed over without further grafting.

DR. H. S. WARD: I enjoyed Dr. Snyder's case reports and congratulate him upon their thoroughness. They are very instructive, and to me are further proof, if it were needed, that pellagra is entirely a disease of improper diet. An exclusive diet of carbohydrates, green vegetables, and "white" or fat meat will produce pellagra. I see a great many cases of pellagra, and if one will take a thorough history and get the real truth of what the patient actually eats—not what was on the table—each can be traced to a "poor folks" country diet of carbohydrates, green vegetables, and fat meat.

I recently saw a real estate man who said that his rental income was $700 per month, and that his family had a liberal diet; but when pressed as to what he really ate, it consisted of: cereals, coffee, syrup, and cakes for breakfast; usually rice pudding or some form of sweets for lunch; bread, butter, syrup and preserves, and coffee for supper. He said that milk, eggs, or meats gave him indigestion. He had definite and well-advanced pellagra—diarrhea, sore mouth, etc. This man had been given sodium cacodylate for months, with the assurance of a certain cure. His diarrhea and other symptoms were getting progressively worse. Diet had not been mentioned to him. A diet of milk and raw eggs only soon made a well man of him.

A mother with two small children, all three with pellagra, gave a history of having been far from a market and had no cow or chickens, so were compelled to live on green vegetables, bacon, and carbohydrates. She and children went to her mother's farm and ate milk and eggs only for three weeks, and returned

to my office. Every apparent symptom of pellagra had vanished. In fact, I did not recognize them at first. These were early acute cases, and responded more quickly to diet than the chronic ones.

Any diet with proteins in excess will perhaps relieve pellagra, but they are all fond of carbohydrates, and it is so easy to take more than is good for them. The only medicine I give in the ordinary cases is dilute nitric acid, if diarrhea is severe, otherwise dilute hydrochloric acid. Observation has shown that pellagrins secrete very little hydrochloric acid, so I feel that this is only supplying a physiologic need. Arsenic is of no value, *per se*, and should be tabooed. Whether the diet theory is correct or not, if it cures, let's give our patients the benefit of it until some one is able to *prove* something that is better.

Dr. W. G. Harrison: Recently while attending a meeting of Medical Directors of One Hundred Life Insurance Companies the question of goiter in its relationship to life insurance was up for discussion, and one of the physicians present who was from eastern North Carolina made some very interesting remarks He said "the death-rate from his company from pellagra was higher than from any other one disease, and that the death-rate in this section of the country from pellagra was definitely higher than from tuberculosis or pneumonia." He spoke of having seen a great many cases of pellagra associated with goiter, and expressed himself as believing that there was some association between the two diseases. He stated frankly that he had no scientific data on which to base his suspicion, but having seen these two diseases associated in so many cases he was asking other men to watch carefully for such connection, and to report if they found similar relationship. I have forgotten his exact statement, but I think he said that he had noticed an association of the diseases in several hundred, maybe more than a thousand, cases.

Dr. Snyder (closing): This report was presented without ambition on my part to settle the etiology of pellagra. Pellagra is a most fascinating study which any one who stops guessing at the etiology will admit. If each of us will investigate every case of the disease that is met with, the accumulating mass of data will sooner or later result in a definite settlement of etiologic

points. If my report will stimulate study among us, I will feel that it has been worth while.

With reference to pellagra being a secondary disease, I want to say this: In malarious districts malaria and pellagra are frequently concomitant diseases; in districts where uncinariasis is prevalent hookworm and pellagra are frequently concomitant; in districts where amebiasis is common pellagra and amebæ are frequently linked together; in some districts corn whisky is the concomitant disease; and tonight we have heard from Dr. Harrison that in some localities goiter and pellagra are concomitant. Now if we happen to be living in one of these districts and do not look over to see what is occurring in the other districts, we are apt to reach the conclusion that pellagra *is* a secondary disease; we are apt to believe that the particular prevailing infection in our locality has a definite etiologic connection with pellagra. But if we broaden our outlook, I think it becomes perfectly plain that neither malaria, nor amebæ, nor hookworm, nor corn whisky, nor goiter has any more definite connection with pellagra than any other enervating and devitalizing agency.

CLINIC OF DR. J. HEYWARD GIBBES

COLUMBIA HOSPITAL, COLUMBIA, S. C.

HODGKIN'S DISEASE

Primary Involvement of Mediastinal Glands with Presentation of Tumor Mass Over Sternum. Blood-picture Characteristic of Well-advanced Disease. Differential Diagnosis. Etiology. Pathologic Anatomy. Prognosis. Treatment.

THIS man is thirty-six years of age, a farmer by occupation. He first came under my observation one week ago, complaining of "swelling on chest, loss of weight, weakness, and cough."

His family and marital history is unimportant.

In his personal history he says that he had measles, whooping-cough, and malaria in early life, and that up to two years ago he drank excessively. He denies all venereal infections, says that he has not been troubled with sore throats, and gives no indications of previous tuberculous infection. He maintains that up to the onset of his present illness his health had been unusually good.

He dates his present illness from twenty months back when he was taken suddenly with a "stitch in the left side" of chest which was intensified by deep breathing. This pain gradually disappeared, but he soon developed a mild but persistent cough, without night-sweats or fever. He very shortly found that he was losing strength and weight. About five months ago his attention was attracted by a swelling over the sternum, extending over toward the left breast, and which he describes as "soft and resembling an abscess." He consulted a physician, who inserted a needle into the mass, but failed to obtain fluid. A few days later an incision into the mass was made and a material expressed

which "looked like brain matter." Since that time he has progressively lost weight, has become increasingly weaker, and has been troubled with a persistent and productive cough. At no time has there been blood in his sputum. The cough is distinctly worse at night and when patient is in prone position.

Upon physical examination we see a man of large frame, evidently emaciated, and with marked pallor of skin and mucous

Fig. 271.

membranes. There is considerable hypertrichosis over chest and forearms. A few purpuric spots are visible over deltoid regions and chest. This large tumor mass presenting just to the left of the midsternum measures approximately 20 cm. in transverse diameter and 4.5 cm. in the other dimension. The superficial ulcerated area on the apex of the tumor represents the site of

incision which has never healed. The tumor is hard, painless, and firmly fixed to the skin. It seems to ramify into the tissues of the chest, especially under the left breast. The lymph-glandular system is of particular interest. The cervicals are easily palpable on both sides, about the size of cow-peas; the axillaries are very large, one mass in the apex of the left axilla being as large as a bantam's egg; the epithrochlears are easily palpable, about 1 cm. in diameter; the inguinals are readily felt. The thyroid is not enlarged, and the spleen cannot be felt. The left supraclavicular fossa is filled with an oblong mass which can be seen at a distance. The signs over the lung area are very striking. You readily see that the respiratory movements are very much limited over the left chest, and that the supra- and infraclavicular fossæ on the left are obliterated. The vocal fremitus is diminished throughout the left chest, being normal on the right. The percussion note is very much impaired throughout the left lung area, especially above the third rib in front and over the suprascapular fossa behind. There is also some impairment of the percussion note over the right upper lobe, merging into a wide area of dulness behind the manubrium, but the note is relatively much more resonant than that over the left upper. There is no flatness over any part of the lung area. The breath sounds are audible throughout both sides of the chest, but markedly diminished over the entire left side. There is evident difficulty to the access of air into the left lung. There is slight tubular modification of the breath sounds over the third interspace in the left front and in the left back at the level of the fifth dorsal spine. No râles heard. On the right side the breath sounds are universally vesicular in quality and much better transmitted than on the left. There is a slight nasal modification of the whispered voice sounds at the level of the third rib in front. The heart seems to be slightly displaced toward the right, but there is no enlargement of the percussion area. There is a soft systolic murmur at the apex which is not transmitted to the axilla, and which doubtless represents a hemic blow. The abdomen presents nothing of note: there is no evidence of collateral circulation, no masses, none of the organs are palpable, and there is

certainly no excess of fluid in the flanks. The lower extremities show nothing of note, but the fingers present a beautiful example of clubbing and watch-crystal nails, the condition classically known as Hippocratic fingers (Fig. 272), and more recently described as a chronic pulmonary osteo-arthropathy.

The sputum is very tenacious, mucopurulent, and abundant, being raised especially in large quantities in the early mornings. Careful studies for tubercle bacilli have been negative. No microscopic or macroscopic blood has been observed.

Fig. 272.—Hippocratic fingers.

The urine is of some interest in that it contains an abundant, granular sediment which disappears on heating and reappears upon cooling—a heavy deposit of urates. These amorphous salts are visible under the microscope, and upon the addition of hydrochloric acid large numbers of uric acid whetstone crystals make their appearance. It is interesting to think that this finding in the urine is probably dependent upon the chronic leukocytosis present in this case, there being a constant destruction of the nuclei of large numbers of cells. Careful heating of the urine in a water-bath failed to disclose the presence of the

Bence-Jones protein. As you doubtless know, this body was formerly supposed to be practically pathognomonic of the disease known as multiple myelomata, a multiple tumor occurring in the bones. But recent studies, notably those of Boggs and Guthrie, from the Johns Hopkins Hospital, have shown that the Bence-Jones body is present in the urine in carcinomatosis of the bones, myelogenous leukemia, and less constantly in cases of lymphatic leukemia. While the condition which we have represented by this patient is not primarily a disease of the leukopoietic tissues, there is at present, as you will see from the report of the blood studies, a functional involvement of these structures, and it would not have been surprising to find the Bence-Jones body in this urine.

The blood of this patient is of great interest because of the variety of cells which it presents an opportunity to observe and because of the statement of Bunting that we find here specific criteria for the making of a diagnosis. You will find a stained preparation under the microscope which I hope you will all look over at the end of the demonstration. The following is a summary of the blood findings:

I. The fresh blood:
   1. No parasites.
   2. No poikilocytosis or anisocytosis.
   3. Red cells much paler than normal.
   4. There is an evident leukocytosis with many coarsely granular cells.

II. Red blood-cells, 3,800,000.

III. White blood-cells, 26,000.

IV. Hemoglobin, 65 per cent. (Sahli).

V. Differential count:

1. Polymorphonuclear neutrophils	925	92.5 per cent.
2. Polymorphonuclear eosinophils	15	1.5 per cent.
3. Polymorphonuclear basophils	00	0.0 per cent.
4. Large mononuclears	19	1.9 per cent.
5. Lymphocytes	23	2.3 per cent.
6. Transitionals	15	1.5 per cent.
7. Myelocytes (neutrophilic)	3	0.3 per cent.
	1000	100.0

In counting these cells 2 nucleated red blood-cells were observed.

We have here a marked secondary anemia, a pronounced leukocytosis, a remarkable relative increase in the polymorpho-

nuclear elements, and a slight relative increase in the eosinophils. Another point of interest and importance, which you may observe in the preparation under the microscope, is the large number of platelets present and especially the unusual size of many of them. Bunting is of the opinion that these large platelets probably are of recent formation through the breaking off of the pseudopodia of the megalokaryocytes in the bone-marrow, and they constitute an important diagnostic link in the chain of evidence to be derived from the study of the blood.

The studies of Bunting and Yates concerning the blood-pictures of Hodgkin's disease are the most interesting observations in connection with this subject since the work of Dorothy Reed put the disease on a sound basis of pathologic anatomy. Among the most interesting papers by Bunting are those published in the Johns Hopkins Hospital Bulletin in 1911, pages 114 and 369, and in the Journal of the American Medical Association in 1915, page 1953. The above blood-picture agrees in detail with that described by Bunting as occurring in the late stages of Hodgkin's disease. The leukocytosis has been found in some instances to reach as high as 100,000.

The Wassermann reaction is negative.

The conjunctival tuberculin tests, 1 and 5 per cent., are negative.

The *x*-ray picture of the chest shows here a dense, broad mediastinal shadow, a marked clouding of the left lower lobe, a more dense infiltration at the level of the upper border of the left scapular, and numerous, well-defined, discrete nodules scattered throughout both lungs, suggesting an involvement of the bronchial lymphatics.

We will now allow the patient to retire.

The condition which we have just seen must be differentiated between:

1. Syphilis.
2. Tuberculosis.
3. Lymphosarcoma.
4. Hodgkin's disease.

The Wassermann, tuberculin reactions, sputum studies, and the

blood studies virtually dispose of the first two conditions. In neither syphilis nor tuberculosis would one expect to find the leukocytosis or the high percentage of polymorphonuclear cells which is present in this case, even in the presence of a secondary pyogenic infection. It would be most unusual to say the least. As regards the possibility of differentiation between lymphosarcoma and Hodgkin's disease in this patient, one must confess to an element of doubt on the basis of clinical evidence alone. We certainly should not be satisfied without the histologic examination of the diseased tissue. The patient has thus far refused to submit to such examinations. Had the patient come under observation in the early stages of his disease, before the leukocytosis had appeared and when the differential blood count may have shown a relative increase in the mononuclear elements, we should probably have had to consider a fifth condition, that of lymphatic leukemia. It is seldom, however, that the blood of Hodgkin's disease approaches the relative mononucleosis seen in lymphatic leukemia. Accepting Bunting's standards of blood interpretation, we may safely conclude that we are dealing here with a truly remarkable example of Hodgkin's disease, the primary involvement having taken place in the glands of the mediastinum.

The **etiologic factors** in this disease are relatively unknown. Renewed interest has been added to this phase of the subject by the work of Bunting. He has succeeded in recovering from the glands and adjacent tissues a non-acid-fast, Gram-positive, diphtheroid organism which he believes to be the causative agent of the disease. He reports the production of a glandular disease in monkeys through the agency of this bacterium, and believes that he has obtained good clinical results from the use of the organism as a vaccine. However, one must await further developments in this connection before finally accepting these views. Pleomorphic, diphtheroid organisms, very similar to those described by Bunting and his co-workers, can frequently be obtained from lymph-glands in other conditions than Hodgkin's disease. In this connection it is well to keep in mind a similar piece of work done with reference to pellagra here: the isolation

of the diphtheroid organism from the glands of patients, its injection into monkeys, and the reported production of a pellagroid condition in these animals. It is to be hoped that Bunting's observations are on a firm foundation, for with their substantiation will come increased information and the possibility of an effective therapy.

The **treatment** of Hodgkin's disease is essentially empirical. The disease is characterized frequently by remissions in which the patient seems to be substantially improved, and it is probable that this may occur independently of therapy. Arsenic seems at times to have a beneficial effect, especially in the form of salvarsan, and it is well to give a few injections of this drug. *x*-Ray treatments over the affected glands should always be practised, needless to say, with discretion. Sustaining measures, good food, proper hygiene, iron in some form in the presence of anemia, and the treatment of symptoms as they arise are practically the only measures at our disposal. The removal of tonsils as possible portals of entry for the exciting agent of the disease and dissection of the affected glands in the early cases have been advocated and may be tried under propitious conditions.

REFLEX GASTROSPASM

Differential Diagnosis Between Functional Spasm and Organic Deformity of Stomach

THE patient that I wish to use as a text for the clinic today is sixty-two years of age. She was referred to me for study by Dr. Guerry, having come to him with the tentative diagnosis of ulcer of the stomach, with probable early malignant change.

I saw her first in August, 1917, at which time she stated that she had been gradually losing strength for about one year. She said that she had been having some little trouble with her stomach for the past ten years, gas, heartburn, and slight pain after eating. For the past four months the pain had been particularly bad, coming on immediately after eating, and the gas had been most annoying. There had been no nausea or vomiting, no hematemesis, and no melena. She had lost about 20 pounds during this period. In addition to this, she complained of pain and burning in the "neck of her bladder."

Her *family history* was unimportant, with the exception of the fact that she had given birth to one still-born child.

The positive points of her *personal* history were: Typhoid fever at twelve years of age, indefinite pains in the joints at times, headaches and dizzy spells occasionally, and the loss of all of her teeth as the result of pyorrhea.

On **physical examination** she was found to have a poor color, and presented evidences of a considerable loss of weight. There was a slight yellowish cast to the skin, but no distinct jaundice. The eyes were not unduly prominent, the pupils were equal and reacted normally. There was a well-marked pterygium on both eyes, more developed on the left. All of the teeth had been removed. The throat was negative. The heart and lungs presented no abnormalities. The abdomen looked natural, no visible masses or peristalsis. The walls of

the abdomen were fairly soft except for slight muscular resistance on palpation over the epigastrium, the patient being distinctly "sore" over the entire epigastric area. This sensitiveness seemed somewhat more marked under the right costal margin. No masses were felt in the abdomen, but an indefinite sensation of a palpable gall-bladder was elicited. The spleen and liver were not felt, and the stomach seemed to be in a high position on auscultatory percussion. The extremities were negative. Vaginal examination disclosed a cauliflower hemangioma just outside of the urethral orifice. The uterus was of normal size and in good position. Her blood-pressure was 160 systolic and 80 diastolic; the pulse 88; and her temperature reached 99° to 99½° F. each day.

The urine showed a specific gravity of 1020, a trace of albumin, no sugar, and a good many pus-cells under the microscope. A catheter specimen could not be obtained because of the obstruction caused by the caruncle.

The stool gave a positive test for occult blood on one occasion, but was negative on other examinations.

Her blood showed 12,000 leukocytes and a hemoglobin of 75 per cent. by a Sahli instrument.

In the gastric analysis we recovered 60 c.c. of an Ewald test-breakfast at the end of one hour. The free hydrochloric acid content was 28 and the total acidity 45. There was no lactic acid present, no blood, and the microscopic examination was negative.

The Wassermann reaction was negative.

The bismuth pictures of the stomach showed a "cow-horn" stomach with incomplete filling of the pylorus and duodenal cap. There was rapid expulsion of the bismuth into the small intestine. The filling defect in the pyloric region was persistent in three pictures.

On the basis of these findings, we felt that we were dealing with a chronic cholecystitis which was giving rise to reflex gastric manifestations, and advised exploration of the gall-bladder and pyloric regions. Operation was performed by Dr. Guerry on the 29th of August, and a well-defined cholecys-

titis with a stone in the cystic duct was found. The stomach presented no signs of pathology. The gall-bladder was removed. With the exception of an acute pyelitis developing the third day after operation, the patient had an uneventful postoperative course.

The patient returned to the hospital on March 25, 1918, for the purpose of having the urethral caruncle removed. She says that she has gained weight since her operation and has been practically free of epigastric pain. She has, however, continued to have a considerable amount of "gas on the stomach" and mild nausea at times. She thinks that she has had some fever each day since leaving the hospital, reaching as high as 101° F. at times.

The physical examination at present differs in no way from that of last summer except for evidences of increase in body weight, the absence of tenderness in the opigastrium, and a palpable right kidney. The gastric analysis shows essentially the same findings, and the persistent low fever is explained by the findings in the urine indicative of a chronic pyelitis.

The *x*-ray picture of the stomach at present is of particular interest, showing in every respect a normal organ, as contrasted with the persistent pyloric deformity which was manifested prior to the gall-bladder operation.

The urethral caruncle was removed by Dr. Guerry on the 2d of this month.

Here we have an illustration of that interesting group of cases in which the presenting symptoms are gastric, and in which these symptoms may be of such a pronounced character as to completely obscure the primary pathologic condition. In this patient the diagnosis of gastric ulcer had already been made and the fear of gastric cancer expressed. The fact that we were able to arrive at an accurate determination of the cause of the gastric phenomena observed in this case does not imply that we are equally as successful in all others, or, in fact, that we generally succeed in differentiating organic disease and functional disorders of the stomach. In collaboration with Dr. R. W. Gibbes and Dr. Guerry, it has been my good fortune to investigate a large

number of patients with presenting gastric symptoms during the past few years, and we have found here a field of unlimited interest and never-ending surprise. In many respects the roentgenographic and roentgenoscopic study of the stomach by means of the bismuth or barium meal is the most exact means of investigating this organ. But this method furnishes us with some of the most confusing data with which we have to contend. This is borne out by the series of pictures that I have just shown you.

These pictures exhibit an excellent example of pylorospasm, with some extension of the spastic condition into the prepyloric portion of the stomach. The frequency of involvement of the distal third of the fundus in these spastic states has suggested the term "gastrospasm," as distinguished from the term "pylorospasm" when the spastic condition is limited to the pylorus. The roentgenologists were not slow in recognizing these so-called "reflex" spasms of the gastric musculature, and an extensive literature has accumulated on the subject. One of the most illuminating articles is by Cole, in the American Journal of Medical Sciences for July, 1914. Practically every one is agreed that it is by no means a simple matter to distinguish at all times between the deformity of the stomach produced by spasm and that resulting from ulcer or tumor encroachment upon the stomach wall. In probably the majority of instances the spastic deformities are inconstant, and serial pictures or fluoroscopic observation will reveal complete relaxation or at least some change in the type or degree of the deformity. But we have now seen a large number of reflex gastric spasms which were so persistent as to defy our efforts at differentiation by means of *x*-ray study. The deformities resulting from ulcer and malignant disease are, of course, relatively much more constant. But gastric spasm frequently occurs in association with organic disease of the stomach, and we have seen this state of affairs so well marked as to render accurate interpretation practically impossible. A point of interest in this connection is the fact that prolonged reflex spasm of the stomach muscle will result in hypertrophy and induration of the wall to such an extent that a permanent deformity will be evidenced in the *x*-ray plates.

Fig. 273.—Picture of normal stomach, showing well-formed pylorus and complete filling of duodenal cap; no filling defects.

Fig. 274.—*x*-Ray picture of stomach, showing spastic condition of pylorus with marked filling defect. Patient with chronic cholecystitis and stone in cystic duct. No pathology at operation.

Fig. 275.—Showing persistence of pylorospasm.

Fig. 276.—Picture of same stomach eight months after removal of gall-bladder, showing normal filling of pylorus and cap.

Fig. 277.—Spastic pylorus in presence of chronic appendicitis and cecal stasis

Fig. 278.—Cecal region and transverse colon with bismuth in appendix.

The symptomatology of reflex gastrospasm or, more properly, of the functional disorder of the stomach which is associated with the gastrospasm, is essentially that of ulcer. I have seen these patients complain of pain immediately after eating, gas, acid eructations, and epigastric hyperesthesia. Others will give a typical story of duodenal ulcer. The symptomatology alone is often of little help. But too much attention cannot be paid to the taking of a systematic and thorough history, enquiring carefully into the present or past incidence of conditions that might give rise to functional disorders of the stomach. These conditions are, briefly: chronic infections in the respiratory tract, oral sepsis, cholecystitis or cholelithiasis, chronic appendicitis, pelvic inflammatory disease, or peritoneal adhesions. Psychoneurotic states may add confusion to the picture.

The physical examination does not always serve to lighten our difficulties. As in the present case, we may be so fortunate as to have it point more or less clearly to a chronic infection in the gall-bladder or appendix region, but too frequently we find the patient with a punctate point of tenderness over the pylorus with a radiation of the pain into the back and a hyperesthesia over the epigastrium. At times the pylorus may be distinctly felt and give the impression of an epigastric mass.

In the majority of these cases the gastric analyses have shown a degree of acidity on the upper limit of normal, a few of them have shown a very high free hydrochloric acid content, and one patient exhibited an absence of free acid. In none of them has blood been found in the gastric contents, but do not lose sight of the fact that slight trauma from the tube might introduce this confusing element. The fractional estimation of stomach contents—*i. e.*, the removal of portions of a test-meal every fifteen minutes after its introduction until the stomach is empty—is putting our knowledge of normal and abnormal gastric function on a more exact basis, and may in time furnish an answer to some of these puzzling questions. But I need only call your attention to the statement of Crohn and Reiss in an article in the American Journal of Medical Sciences for December, 1917, to the effect that they have been unable to differentiate the

curves of gastric acidity seen in cholelithiasis and chronic appendicitis from those found in ulcer of the stomach.

Repeated examinations of the stools for occult blood is of decided help in differential diagnosis. Repeatedly negative tests for occult blood are most valuable in attempting to eliminate gastric ulcer or cancer from consideration. But bear in mind that positive tests are of much less significance. The diet should be practically hemoglobin free, and the nose, pharynx, buccal mucous membrane, and rectum investigated as possible sources of blood before a positive test is allowed to carry its full weight.

In my experience the most helpful single examination has been a leukocyte count. The cases of reflex gastric spasm associated with chronic cholecystitis, chronic appendicitis, or chronic pelvic inflammatory disease have all shown a mild leukocytosis. But here again one must keep in mind the possibilities of error. A gastric ulcer is frequently the seat of secondary infection, and a high leukocytosis is often associated with malignant disease.

Gastroscopy has not come into general clinical use as rapidly as one might have expected, doubtless because of the technical difficulties incident to its application. In the opinion of such men as Janeway, of New York, and Jackson, of Pittsburgh, this procedure furnishes very exact information concerning the cardiac end of the stomach, and they think that it takes precedence over all other means of investigating this portion of the organ, just as the *x*-ray does for the pylorus. Not infrequently it is necessary to give an anesthetic for the introduction of the gastroscope, but in careful and experienced hands the method can be carried out with perfect safety. While reflex spasm of the cardia is much less frequently encountered than pylorospasm, it does occur at times, and direct vision should enable us to eliminate organic disease from consideration.

I wish to call your attention briefly to another group of cases, the exact pathology of which is very uncertain, which present manifestations readily confused with ulcer or which might frequently be interpreted as a reflex gastrospasm. During the past eighteen months I have seen 4 patients with typical

Fig. 279.—Patient eighteen years of age; history suggestive of gastric ulcer with four plus Wassermann reaction. Condition thought to be ulcer until report on Wassermann was obtained.

Fig. 280.—Showing persistent pyloric defect in above case.

Fig. 281.—History and findings indicative of duodenal ulcer and chronic cholecystitis. Both conditions found at operation.

Fig. 282.—Partial relaxation of pylorospasm. This patient showed a hypertrophy and induration of stomach wall resulting from chronic spasm.

ulcer histories, 2 of them having hyperacidity findings in the gastric secretions, one a hypo-acidity, while in the fourth no gastric analysis was obtained. All of these patients gave positive Wassermann reactions, and their stomach symptoms promptly disappeared under salvarsan and mixed treatment. You will note in one of the pictures here a persistent filling defect in the fundic portion of the stomach, while the other case shows a deformity in the pyloric region which was regarded as a reflex spasm until the Wassermann report was obtained. Unfortunately, we have been unable to get pictures of these stomachs since the administration of treatment. We hope to do so in the near future, and it will be interesting to see what changes have taken place. It is quite possible that these cases represent an actual syphilitic ulceration of the gastric mucosa, either as mucous patches or as ulcerative degeneration of gummata. Proliferative infiltration of the gastric wall and cicatricial deformity of the lumen have been observed at operation on patients with syphilis of the stomach. The routine application of the Wassermann reaction is leading to the discovery of more and more gastric syphilis. Take the temperature and take the pulse, but also take the blood for a Wassermann reaction, is advice that we all might follow with advantage to ourselves and to our patients.

I hope that I have shown you some of the difficulties of gastric diagnosis. In possibly the majority of cases it is possible to differentiate between functional and organic conditions, but a considerable number of cases will defy this distinction. Given this primary decision, say, for example, that we recognize an organic deformity of the stomach in a certain case, the differentiation between benign ulcer and malignant disease is a relatively simple matter. But you will find, no matter how careful and exhaustive your investigations may be, that you will mistake functional spasm for organic deformity many times, and vice versa. The greater number of reflex gastrospasms result from intraperitoneal pathology, especially chronic cholecystitis, chronic appendicitis, and pericecal adhesions, and all of these conditions are to be looked upon as surgical when

associated with profound derangements of gastric function. I think you might accept the following as a safe rule: A history of gastric malfunction, gastric secretory findings deviating from the normal, an *x*-ray plate indicating anomalies of motor function in the stomach, and the elimination of extraperitoneal causes of gastrospasm, together with a negative Wassermann reaction, represents a group of clinical data indicating the necessity for exploration of the peritoneal cavity.

CONTRIBUTION BY DR. WILLIAM H. DEADERICK

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THE TREATMENT OF MALARIA

IN the treatment of malaria we possess a drug which is probably the type of specifics, quinin. Most of the salts of quinin are readily absorbed from the stomach. It has been shown, however, that the tannate is more largely absorbed from the small intestine. The rapidity of absorption varies with the different salts and is estimated by the length of time required to appear in the urine. This varies from fifteen minutes with the hydrochlorid to three hours with the tannate.

The method of administration of quinin influences the rapidity with which it is absorbed. Given by mouth, a highly soluble salt will begin to appear in the urine within fifteen to thirty minutes, and is eliminated in the greatest quantity within three to twelve hours. Employed hypodermically, the rapidity and thoroughness of absorption depend upon the solubility of the salt and the concentration of the solution. The latter is of the utmost importance, since no matter how soluble the salt, if given in concentrated solution it will not be absorbed. After intravenous administration quinin may be detected in the urine in ten to twenty-five minutes.

The action of quinin upon the malaria parasites is that of a protoplasmic poison, and is most powerful against the spores before they have assumed the protection of the red blood-cells. While young and half-grown tertian and quartan gametes are sometimes destroyed by quinin, those of the estivo-autumnal variety are exceedingly difficult to kill. In rare instances small doses of quinin appear to arouse latent malaria, a provocative

reaction, and in isolated cases there is no doubt that the parasites acquire a relative immunity to the drug and become quinin-fast.

The mere statement of the patient that he is unable to take quinin should constitute no bar to the use of the specific. However, cardiac depression and dyspnea are decided contraindications to the administration of the drug. Happily, such cases are rare. In a long experience in a highly malarial locality I encountered only two.

The treatment of malaria complicating pregnancy is essentially the same as under other conditions. The history of blackwater fever is no contraindication to the use of quinin. While the administration of the drug is sometimes the occasion of an outbreak of hemoglobinuria, the latter is generally due to too little quinin rather than too much.

The dihydrochlorid is the most valuable salt of quinin, inasmuch as it is very soluble, causing fewer nervous or gastric symptoms in the patient and being very poisonous to the parasite. It is, furthermore, the most suitable preparation for intramuscular and intravenous administration. The sulphate is useful in the treatment of malaria in children, being fairly palatable in suspension in aromatic syrup of yerba santa. Euquinin is almost tasteless and has given satisfactory results in my hands. Tannate of quinin, on account of its small proportion of alkaloid and slight solubility, has been rarely employed in this country in the therapy of malaria. However, my own experience with this salt, together with the reports of the Italian physicians, leads to the following conclusions:

1. The tannate of quinin is almost completely absorbed from the alimentary tract.

2. It is more slowly absorbed and more slowly eliminated than the other salts of quinin, and remains in the system longer.

3. A small quantity only of the salt is acted upon by the gastric juice, but is largely absorbed from the bowel after contact with the bile and pancreatic juice.

4. It is not absorbed when injected into the rectum.

5. It is better tolerated by the stomach, intestines, and nervous system than the sulphate.

6. The clinical results with the tannate of quinin are entirely satisfactory.

7. Being nearly tasteless, it is especially adapted to the treatment of malaria in children.

8. It has a good effect upon diarrhea and dysentery complicating malaria.

9. It is several times less expensive than any other tasteless preparation of quinin.

In simple cases of malaria administration of quinin by the mouth is the rule. The ideal form by this method is the solution, but the taste is so repugnant that this form has never been widely used except in hospital practice. Pills and tablets are convenient to administer and not unpleasant to take, but cannot be relied upon. The coating often becomes so hard as to make solution difficult or impossible. Capsules, when fresh, are easily dissolved. The most suitable salt of quinin for injection is, unquestionably, the dihydrochlorid.

The advantages of giving quinin by the needle in pernicious malaria are obviously being able to administer it to patients unable to swallow or to retain it and the certainty and promptness of absorption. The necessity of employing a dilute solution is of the first importance. Strong solutions of quinin injected into the tissues cause a wall of necrosis around the solution, preventing absorption and paralyzing phagocytosis, resulting, even if the solution is sterile, in nodes or ugly chemical sloughs. A solution for intramuscular injection should not be stronger than 10 per cent. The solutions should not be injected hypodermically, but intramuscularly, since in the latter location the injection is more certainly absorbed, is less apt to cause induration and abscess, and is less painful. The initial dose should ordinarily be 10 or 15 grains. Afterward from 5 to 10 grains should be injected every six to eight hours as long as the symptoms demand it. The best location for injection is in the gluteal region and above the ischial tuberosities.

The intravenous method is coming into more general use, and deservedly so. The technic usually employed is similar to that used in the intravenous injection of salvarsan. However, those

adept in intravenous technic may use a 10 per cent. solution of the dihydrochlorid. A convenient apparatus consists of two 10-c.c. Luer syringes, connected by a stop-cock, one holding the quinin solution, the other normal salt solution. As soon as the vein is entered the plunger of the salt syringe is gently withdrawn, and when blood appears in the syringe the salt solution is slowly injected to make sure that the puncture is satisfactory, in which case the stop-cock is turned and the quinin is slowly injected. Some of the pharmaceutical houses are now putting out ampules containing quinin in sufficiently dilute solutions for immediate use without the addition of water or other diluent. These will undoubtedly prove life-savers in the hands of many physicians who have not immediate access to facilities for preparing solutions for intravenous injection. The intravenous injection should be the method of choice in the administration of quinin in cases of pernicious malaria, cases showing serious symptoms, or where there is any doubt that the drug will be retained if administered by the mouth. Rectal and epidermic administration are to be regarded merely as adjuvants in the treatment of malaria.

With reference to the time when the drug is given there are three chief modes of giving quinin: (1) The method of Torti, a single dose before the paroxysm; (2) the method of Sydenham, a single dose in the decline of the paroxysm; and (3) the method of fractional doses. The third method, that of small doses at frequent intervals, has numerous advantages over the one-dose methods.

1. Quinin given in this way is better borne by the digestive and nervous systems.

2. The loss of one dose by vomiting or failure of absorption is not of so much importance.

3. The method is adapted to tertian, quartan, or estivo-autumnal infections; this is important, for sometimes these cannot be differentiated clinically.

4. It is adapted especially to estivo-autumnal infections where sporulation is not so nearly synchronous.

5. The time of administration is not dependent on parasitic

findings or definite stages, both of which may be obscure where the patient has previously taken quinin.

6. An experience in many hundreds of cases has proved its value.

I give quinin in this way almost exclusively. The average dose is 1 grain an hour, given usually 2 grains every two hours, 3 grains every three hours, or 4 grains every four hours, day and night. It is especially important that the drug be given during the night, since thus only may the blood be charged during the day, when sporulation occurs. Cinchonism is no guide to the quantity to be given; it is not the patient toward which the quinin is directed, but the parasite.

The specific should not be discontinued as soon as the temperature is normal, but should be kept up for at least two days longer in the quantity employed during the fever. Thereafter about 15 grains on two successive days of each week should be given for at least two or three months to prevent relapse, even though the patient leave the malarial locality. A few days' treatment with quinin no more cures malaria than does a few weeks' rubbing with mercury cure syphilis.

As to the hygienic treatment this varies in no way from that of other acute fevers. It is customary to begin the medical treatment with a purge. Calomel is the drug most easily administered and retained. The dose need not exceed 5 or 6 grains and the quinin should not be delayed for the action of the purgative. During the cold stage, blankets, hot drinks, and the external applications to the head, tepid sponging, and cold rectal injections may be used. The coal-tar antipyretics are not often indicated. Cold drinks may be given.

For the headache, cold applications, codein and acetanilid, or chloral and bromid of soda are useful, and if the pain demands it, morphin need not be withheld. If nervousness is marked the monobromated camphor should be administered with the quinin in capsules, or the bromid of soda, in solution, with each dose of the specific. For vomiting, if intense and not relieved by the application of a mustard plaster to the epigastrium, morphin should be employed subcutaneously.

After successfully meeting the active symptoms of quinin, administered as above outlined, the prevention of a relapse is to be accomplished by giving 15 grains of quinin every sixth and seventh days for a period of not less than two or three months. The administration of a valuable salt of quinin in this manner has rarely failed, in my experience, to cure the most obstinate case of chronic malaria. The quinin is usually given in 3-grain doses every three hours until five are taken.

Nothing is more discouraging to the physician than the treatment of cachectics in whom the poor hygienic conditions cannot be corrected, which is not rarely the case. The two chief principles involved in the treatment of cachexia are: first, the prevention of active outbreaks of malaria, and, second, the improvement of the general condition of the patient by appropriate hygiene. Quinin is most effectively given upon two successive days in each week as described. This alone, however, will rarely effect a cure except in the mildest cases.

Where it is practicable a complete change of climate should be advised. Without this very little can be accomplished for cases of severe degree. A wholesome, nutritious, and digestible diet should be prescribed. The digestion is often impaired and stomachic tonics may be indicated. Exposure to inclement weather must be avoided on account of the dangers of pneumonia. Occupations which subject the cachectic to violent exertion or to bodily harm should be interdicted for fear of rupture of the spleen. Regular hours must be kept and constipation overcome.

Of drugs other than quinin, sodium cacodylate in 3-grain doses daily have given me the best results. Iron is nearly always indicated; the preparations of organic iron with manganese are best tolerated by the stomach.

In the treatment of malaria there is no drug that can compare in efficiency to the salts of quinin; nevertheless, in rare instances it becomes necessary on account of idiosyncrasy to resort to the use of other remedial agents. While the newer preparations of quinin—euquinin, saloquinin, aristochin, etc.—are purported to be free from the toxic properties of the official salts, I have seen one case in which euquinin caused distressing dyspnea, and

another case in which this preparation caused violent urticaria. Euquinin is probably the most valuable of these preparations.

Methylene blue seems to possess some specific action upon the parasites of malaria. The dose is from $1\frac{1}{2}$ to 3 grains given every three hours until from $7\frac{1}{2}$ to 15 grains have been given in twenty hours. The patient should always be forewarned of the blue color imparted to the urine and feces.

There is no doubt that salvarsan cures some cases of malaria where all other means fail. Such cases are doubtless those in which "quinin-fast" organisms are present. The drug should be administered by the usual technic in ordinary dosage at weekly intervals.

In pernicious attacks the quinin should always be administered intravenously where this is possible, otherwise the intramuscular route must be chosen.

CLINIC OF DR. ROBERT WILSON, JR.

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A CASE OF GONOCOCCEMIA

THE patient before us is a young white man about twenty years of age; married. His occupation is that of boilermaker, and at present he is employed at the Charleston Navy Yard. He gives a history of having had the diseases common to childhood, but no other serious illness, and denies both syphilis and gonorrhea.

His present illness began about a week ago, with a rather abrupt onset. He was seized while at work with a severe pain in the lower part of the abdomen on the right side. The pain became so great that he was forced to stop work and return home. On the following day the right epididymis became involved and twenty-four hours later he experienced pain in the right elbow. This was followed by pain in the left knee, then in the left elbow, the pain being quite intense at first. The next symptom noticed was a red line extending along the inner side of the left arm, from just below the elbow to about 1½ inches above. The left supraclavicular glands then became swollen. Finally, the right knee became affected. The wrists and hands shared in the involvement, the fingers becoming very stiff and somewhat painful. There was no swelling of any of the joints. The muscles of both extremities at this time became very painful, so that the mere weight of the bedclothes caused considerable suffering, the gastrocnemius being especially affected. Four days after the onset of the illness he found that he was unable to raise his hands at the wrists, the feet being similarly affected. For the first three or four nights his temperature was quite

high, ranging from 103° to 104° F., and he was very delirious, being kept in bed with difficulty.

When he entered the hospital on February 10th his temperature was 99.4° F., pulse 104, respiration 26. He was suffering very much and was given codein sulphate, ½ grain, by hypodermic. During the night he was very restless and slept very little. For the next two days his temperature ranged from 98° F. in the morning to 100.4° F. in the afternoon. The pulse-rate increased progressively, but has not been above 126 at any time. The respiratory rate has also increased moderately, being at present 32. His mind has been clear most of the time, but this morning he has been quite irrational. Insomnia has been persistent. He has been somewhat nauseated, but has not vomited. Bowel movements have been involuntary for the last two days, but there is nothing characteristic about the stools. The urine is scanty; it is acid in reaction, has a specific gravity of 1012, and contains a large amount of albumin, a trace of indican, a few leukocytes, and some hyaline and granular casts; there is no sugar, no acetone, and no blood. Two examinations of the blood are recorded, made respectively on the morning and the afternoon of the day following admission. The result of the first examination was as follows:

Hemoglobin, 85 per cent.; leukocytes, 34,360; small lymphocytes, 12.75 per cent.; large lymphocytes, 3 per cent.; large mononuclears, 0.50 per cent.; polymorphonuclears, 83.75 per cent.; eosinophils none; basophils none.

The result of the second examination was as follows:

Hemoglobin, 85 per cent.; leukocytes, 54,981; small lymphocytes, 4.75 per cent.; large lymphocytes, 2.25 per cent.; large mononuclears none; polymorphonuclears, 93 per cent.; eosinophils none; basophils none.

No plasmodia were found on either examination.

On examination the patient exhibits evidence of suffering much pain, and the skin and muscles of the arm, leg, and abdomen are exceedingly sensitive; the gastrocnemius is considerably swollen as well as painful. The abdomen was quite distended when he was admitted, which condition has steadily

increased until the present moment, when it is very pronounced. There is some resistance, especially on the right side, but this seems to be due to the superficial sensitiveness. This sensitiveness renders palpation of the abdominal organs rather difficult, but there does not appear to be any enlargement of the liver or spleen. There is no swelling of any of the joints, but all are very painful. Multiple neuritis is present, involving both the upper and lower extremities. Wrist-drop is quite marked, but paralysis is not complete, the patient being able to raise the hand slightly with much effort. Foot-drop is less pronounced. The tendon reflexes are not abolished. The pupillary reflexes are normal. There is no enlargement of the lymph-glands with the exception of those of the left supraclavicular region, which are still swollen. The epididymis is swollen and tender. There is a very slight discharge of clear mucus from the urethra. The apex of the heart is in the fifth interspace, $3\frac{1}{2}$ inches to the left of the midsternal line. The valve sounds are clear and distinct, no adventitious sounds being heard at any area. The pulse is strong and full. The arteries appear to be normal. Nothing abnormal is found on physical examination of the lungs. The tonsils are slightly enlarged and the mucous membrane of the fauces and pharynx somewhat inflamed. No cutaneous eruption of any kind is visible. There is no muscular rigidity.

It is very evident that the patient is suffering with a severe acute infection. The very high leukocyte count suggests possibly that the infecting agent might be the pneumococcus or the meningococcus, although there is an absence of any evidence of involvement of either the lungs or the meninges. The epididymitis very strongly suggests the probability that the gonococcus may be responsible for the infection, although the patient denies ever having had gonorrhea, and no evidence of urethritis is present beyond a very slight mucous discharge. In order to clear up the nature of the infection a blood-culture was made by Dr. Mood, who reports the presence of a Gram-negative coccus morphologically identical with the gonococcus and agglutinating with gonococcal serum, but showing no agglutination with other sera, including the polyvalent meningococcal serum of the

Rockefeller Institute. He believes that there is little doubt that the organism is the gonococcus. The case before us, therefore, is one of gonococcemia.

Gonococcemia is a well-recognized condition. The occurrence of metastases in the joints had rendered the invasion of the blood-stream evident, but the first definite proof was furnished by Hewes, who in 1894 succeeded in isolating the organism from the blood in a case of arthritis. Subsequently, in 1896, Thayer and Blumer obtained a pure culture of gonococcus from the blood of a patient suffering with endocarditis, and after death were able to cultivate the organism from the vegetations on the valves. Since then the gonococcus has been obtained from blood during life a number of times. Faure-Beaulieu in 1906 reviewed 34 cases, and Cole has analyzed 29 cases in which blood-cultures had been made during life. Loforo gives his own findings in an investigation of 67 cases. Of these, "39 gave positive results." He found the gonococcus present in 19 out of 26 cases complicated with epididymitis, and in 11 out of 19 cases of chronic urethritis. In 8 cases examined within the first thirty days his results were negative. It is impossible to avoid the conclusion that gonorrhea becomes a systemic infection far more frequently than we have been prone to think.

The portal of entrance is the affected mucous membrane. As J. Aldington Gibb remarks, "there are three stages in the spread of gonococcal infection: (*a*) urethral infection; (*b*) blood invasion, and (*c*) tissue invasion." Loforo believes that the organism reaches the blood-stream through the lymphatic system, but David Watson is of the opinion that while this may be true in many cases, "in others direct entry into a blood-vessel associated perhaps with venous thrombosis is the origin of the systemic infection."

It is important to note that some of the cases, as, for example, one reported by Nicoll and Wilson, showed no signs of urethritis and gave no history of gonorrhea. The case before us gave a negative history, but does show some signs of a slight mucous discharge. In this connection it may be noted that attention has been called to the fact that coincidentally with the onset of

acute symptoms of general infection, with chills, fever, etc., the urethritis may disappear. Watson points out that "it should not require a knowledge of the presence of a concurrent gonorrhea to direct attention to the possibility of the gonococcus being the offensive agent in an obscure septicemia. The gonococcus being one of the most common disease producers, all blood examinations for unknown infecting agents should include a search for this germ."

Cases of gonococcemia may be grouped into (*a*) those whose symptoms are purely toxic; (*b*) those with metastases. The former are less frequent than the latter and may easily be overlooked. In the symptoms and course they may resemble pyemia, typhoid fever, or malaria, and the diagnosis depends solely on the blood-culture. In one of Thayer's cases the patient presented "vague, general symptoms of headache, backache, and general malaise, continued fever, a thickly coated tongue, a palpable spleen, and suspicious rose spots," strongly suggestive of typhoid fever. Widal tests were negative and blood-cultures showed gonococci. This patient had an active gonorrhea at the time.

Of the metastases, "the most frequent is arthritis, the most important endocarditis" (Watson). Arthritis is usually polyarticular and may or may not be associated with effusion. It may happen that a history of trauma or of antecedent rheumatism is obtained, in which case these conditions probably exerted an influence in reducing local resistance, and in this way determined the point of lodgment.

The association of endocarditis with gonorrhea was pointed out by Ricard as long ago as 1847, and Brandes in 1854 further emphasized this possibility. Attention already has been called to the proof afforded by Thayer and Blumer that the gonococcus is undoubtedly a cause of endocarditis. Most of the cases reported have been associated with arthritis, but this is not to be regarded as an essential concomitant. It does not seem to be a very frequent complication, although Faure-Beaulieu found in his series only 3 cases in which there was no evidence of endocardial localization, and Cole found that in 11 cases of his series there were signs of endocarditis, and in only one of these was

the endocarditis of moderate grade. In 49 cases analyzed by Kühls the aortic valve was affected 28 times, the mitral 8, and the pulmonic 6, the remaining cases showing combined lesions. In several of the cases of endocarditis which have been reported pericarditis has coexisted. Pericarditis alone has been reported in a number of instances.

There is practically no mucous or serous surface which has not been the seat of gonorrheal infection. Epipidymitis, metritis, salpingitis, peritonitis, pleuritis, meningitis, conjunctivitis, and iritis are among the more or less familiar complications.

Enlargement of the spleen may occur. According to Irons, it was reported to be present in 15 and absent in 4 out of 42 cases of undoubted gonococcemia. The liver is very rarely involved, but icterus has been reported.

The kidneys may be involved by direct extension, by metastasis, especially in the endocarditis cases, and probably in the purely toxemic cases there may be toxic albuminuria.

A variety of skin lesions has been noted, including different forms of erythema. Petechiæ have been observed in some cases, and in the case reported by Thayer, above quoted, a typhoid-like rose-rash was present. Others have reported similar cases. Lenhartz, Thayer, and Irons have observed herpes labialis.

The blood shows a polymorphonuclear leukocytosis, usually very pronounced. In one of Irons' cases a leukocytosis of 40,000 was present.

Multiple neuritis has been reported in some cases. It may be purely toxic in origin, but not necessarily so. It is usually seen in association with metastases.

Delirium and stupor may likewise occur as toxic manifestations, or as the result of meningeal localization.

The case before us is one of unusual interest as presenting so many of the phenomena of systemic gonorrheal infection. Whether he has suffered with an attack of gonorrhea recently and disguised the fact, or whether he had a mild chronic posterior urethritis or prostatitis resulting from an old infection, cannot be ascertained. It may be mentioned for what it is worth, that he has a healthy baby eight months old and that his wife has

never manifested any symptoms of gonorrhea. The beginning of the present illness may have been due to a localization in the vas deferens at the point where it curves around the deep epigastric artery, at which point perhaps there developed also a localized peritonitis. The epididymis may have become involved by extension along the vas deferens from the point of the first infection. Or perhaps, as suggested by Prof. Phillips, the initial pain may have been reflex from a primary acute inflammation of the prostate or of the seminal vesicles. Systemic infection with metastases quickly followed; arthritis, lymphangitis, and cervical adenopathy occurring as metastatic phenomena. The neuritis and delirium were probably purely toxic. The very marked sensitiveness and swelling of the muscles of the extremities and abdominal walls were probably due to diffuse myositis, a gonorrheal form of which has been pointed out by Eichhorst, Ware, and others.

CLINIC OF DR. JAMES E. PAULLIN

ATLANTA, GA.

MYOCARDIAL INFARCT FOLLOWING CORONARY SCLEROSIS

THE patient presented to you today has been in the hospital on three previous occasions—his first admission was January 15, 1916; the second admission, November 10, 1916; the third admission, July 21, 1917; and his present admission, March 18, 1918.

Briefly summarized, his previous record is as follows:

First admission, January 15, 1916: Mr. X, white, male, married, sixty-five years of age; merchant.

Complaint, shortness of breath and cold.

Family history unimportant.

Past History.—Patient states that he has always enjoyed the best of health, has had little or no sickness during his life; he remembers having had measles and pertussis in childhood, but no other of the infectious diseases. He denies any venereal disease.

In 1910 he suffered with an attack of indigestion (?), which was really the first illness of any moment severe enough to make him consult a physician. He states that the manifestations of indigestion which he had at this time were sour belching, regurgitation of food, and a great deal of flatulence, most noticed from one-half to one hour after eating, and an uncomfortable sensation of fulness in the epigastrium. This particular ailment followed an attack of grip which did not confine him to bed. He gradually recovered from the indigestion by restricting his diet, getting out of doors, drinking water, and taking exercise.

About two months after recovering from his indigestion in 1910 he was rejected for life insurance because of the presence of

albumin and casts in his urine. He was told at the time that he had Bright's disease, but he did not believe it, and has received no treatment for this trouble up to the present time.

Present illness began about the middle of November, 1915, when he contracted a severe cold. He had some fever, with aching over his entire body, which after a few days was followed by severe paroxysms of coughing, with expectoration of very little sputum. Two or three weeks after onset he began to expectorate a considerable quantity of thin yellow tenacious material which had no odor, and was most marked in the early morning. The attack lasted, with very little improvement, for six or eight weeks. During the latter part of this illness he complained a great deal of shortness of breath, which would come on in nocturnal paroxysms lasting from one to two hours; the paroxysms were exceptionally aggravating and would be followed by drenching sweats and marked prostration. He was not confined to bed, however, any of this time. At present he suffers with marked dyspnea on exertion, attacks of nocturnal dyspnea, cough, worse at night, palpitation of the heart, and general weakness.

Habits.—Sleeps from 11 P. M. to 4 or 5 A. M. As a general rule he sleeps well, although of late he has been disturbed by attacks of dyspnea. He eats very heavily of meat and drinks two cups of coffee daily. Does not use tobacco; takes an occasional drink of whisky. Appetite very good. Bowels act daily without purgatives. Rises from one to three times at night to urinate. Works from 6.30 A. M. to 10 P. M., with short intermissions for meals. Very little or no out-of-door exercise.

Physical Examination.—Patient is well developed, mediumly nourished, fairly well preserved for his years. Skin has a decidedly pale, pasty color, slight cyanosis of his lips and fingertips, respirations are quick, short, and shallow as he sits or reclines. Temporal arteries are quite tortuous; the brachial, axillary, and temporal arteries can be seen to pulsate. Respirations 36 to the minute—a bit labored and shallow. Gums and mucous membranes are a trifle pale. Pupils are equal, react to light and accommodation; eye movements are normal, no con-

traction of the field of vision; the retinal vessels are quite tortuous, veins distended, disks normal. Teeth are in fairly good condition. Tongue is heavily furred, protruded in the median line, breath quite foul. Tonsils are not enlarged, pharynx red and congested. Ears are normal. There is no general glandular enlargement. No enlargement of the thyroid.

Chest is well formed, barrel shaped, expansion is limited, equal on the two sides, costal angle is about 110 degrees; no bulging of the interspaces; no pulsation is observed over either the anterior or posterior portion of the chest. The percussion note over the entire chest is hyperresonant; no increase of vocal fremitus. On auscultation the breath sounds are quite distant; numerous large and medium dry râles can be heard over the entire chest.

Heart.—P. M. I. both seen and felt in the fifth is 10 cm. from the midsternal line; dulness extends to this point; no thrill is palpable. Apex-beat is full and is quite forceful, no increase of cardiac dulness to the right, no increase of substernal area of dulness. At the apex both sounds are loud and snapping. A^2 is decidedly louder than P^2, there is no murmur. Pulse is full, bounding, 90 per minute, regular in force and rhythm; vessel wall is easily felt and quite atheromatous; systolic pressure 210, diastolic 114.

Abdomen shows nothing of importance.

Genitalia normal.

Extremities normal. Reflexes are present; not exaggerated.

Blood Examination.—Red cells, 4,864,000; white cells, 6200; hemoglobin (Sahli), 95 per cent. Stained specimen showed nothing abnormal. Wassermann reaction negative.

Urine.—Single specimen, specific gravity 1025, decided trace of albumin, no sugar, quite a number of hyaline and granular casts.

Phthalein Test.—The dye appeared in twelve minutes: 25 per cent. excreted the first hour, 15 per cent. the second hour.

The patient remained in the hospital at rest for four weeks on a restricted diet, his condition greatly improved, all of his subjective symptoms disappearing.

Second admission, November 10, 1916.

Since the patient's discharge from hospital he continued to improve until October, 1916, when he states that he contracted a severe cold. He states that he got quite warm while cranking his automobile, and shortly after getting back in his car he had a rather sudden pain in the left side of his chest which ran down the left arm. He thinks the pain was due to riding after getting warm from the exercise which he had taken. Following this he began suffering with cough, shortness of breath, expectoration of a thin mucoid material; his cough was much worse in the afternoon and evening than at any other time. Occasionally during the night for the past ten days he has been awakened from a sound slumber with attacks of dyspnea, and he has suffered since the onset of this attack with considerable tightness in his chest, which he thinks keeps him from getting a long breath. He tires very easily and is unable to walk any distance without great discomfort, pain, and tightness in his chest.

On **physical examination** at this time his respiration is 32 per minute and rather shallow. Quite a number of loud, coarse, high-pitched, dry râles are heard over the entire chest and a few fine moist râles at the bases of both lungs.

Heart.—Apex rather diffuse; P. M. I. in fifth is 11 cm. from the midsternal line; sounds at the base and apex are clear, although there is a tendency toward muffling of the first sound. The second aortic is markedly accentuated. Pulse 100 to the minute, slightly irregular, due to premature contractions. Blood-pressure: systolic 200, diastolic 124.

The twenty-four-hour output of urine was 800 c.c., specific gravity 1030, albumin very heavy, microscopically contained numerous granular and hyaline casts and a few red blood-cells.

On the third day of his stay in the hospital there developed over the left side of the chest posteriorly an impairment of the percussion note extending from the angle of the scapula downward over the lower portion of the chest; vocal fremitus was absent over this area, and the breath sounds were quite distant. Over the upper portion of the left lung one could hear any number of fine moist râles; the right lung was apparently normal. Temperature was normal. Chest was aspirated and about 200

c.c. of a clear straw-colored fluid were removed; this was bacteriologically sterile, and a guinea-pig injected with the fluid did not develop tuberculosis.

On a restricted diet, rest in bed, and the administration of digitalis the patient's condition gradually improved until he was discharged from the hospital December 15, 1916.

Third admission, July 21, 1917.

Since last in the hospital patient has been able to do very little; he has suffered more or less constantly with dyspnea and attacks of severe substernal pain, radiating to his left and right arms. Accompanying the pain he has had a marked sensation of depression and has been quite despondent. The attacks of pain would last from five to fifteen minutes; they have increased in frequency and severity, so that at the present time he has from three to four attacks during the twenty-four hours. The pain is brought on by physical exertion or excitement of any kind.

On **physical examination** at this time the heart has increased in size, the apex being 12½ cm. from the midsternal line. It is not so forcible and is more diffuse than it has been on previous occasions. There is a slight increase in cardiac dulness to the right. The first sound is decidedly muffled, is followed by a soft, blowing, systolic murmur, which is heard over the entire precordium. The second aortic is loud and snapping. There are a few moist râles at the bases of both lungs, otherwise very little is made out in the chest. The liver is two fingerbreadths below the costal margin, rather hard and firm, not particularly tender.

The urine is scanty, highly colored, contains a considerable amount of albumin, and quite a number of hyaline and granular casts.

After six weeks' rest in bed, graduated exercise, and other remedial measures for this condition the patient improved considerably, and he was allowed to return to his home.

Present admission, March 18, 1918—the patient states that since his discharge from the hospital he was very comfortable for a greater portion of the time and got along very well until March 16th, when he was awakened from a sound sleep suffering with most intense pain in his chest. This pain was much severer

than the previous attacks which he had had, and lasted without intermission, except for relief by the inhalation of chloroform, approximately six hours. He states that had his chest been in a vise and this tightly screwed up he could not have suffered any more than he has. Following the six hours of intense agony he says there was some relief in the severity of his pain, but it did not completely disappear until he commenced his journey to the hospital, when the pain suddenly disappeared; with this disappearance he was fairly comfortable for two or three hours, when his right leg suddenly became numb and he had a sensation of pins and needles sticking in his foot and the calf of his leg. He states that he could walk on the leg, but that he was very much afraid of paralysis.

On **physical examination** at the time the patient was admitted to the hospital he was extremely restless, tossing from side to side in his bed, markedly dyspneic, lips and finger-tips cyanosed, his expression extremely anxious, and he complained of a numbness and tingling in his right leg. Pulse was 90 to the minute, regular in force and rhythm, full and bounding, systolic pressure 240, diastolic 110. The heart apex 12½ cm. from the median line, forceful, and diffuse. Both sounds were clear, loud, and snapping. The lungs show nothing of moment.

The right leg below the knee was cold and clammy; no pulsation could be made out in the dorsalis pedis, popliteal, or in the femoral artery. There was no loss of motion, no loss of strength, and sensation was intact. The patient was given his first dose of morphin at this time, which, instead of quieting him, increased his restlessness to a marked extent.

On March 19th a beginning dark reddish discoloration of the right foot was observed; this has rapidly increased from day to day until, as you see him now, the discoloration is clearly defined, involving the entire lower extremity and extending for a distance of 16 cm. above the patella. You will also notice that there is a marked difference between the appearance of the toes, and that portion of the leg above the knee. You will notice that the toes seem to have dried up almost completely; the skin is clear and transparent and the tendons and bones are easily seen through

the skin; there is also considerable difference between the size of the feet, the right being smaller than the left. The patient is still able to partially flex the right leg, but there is no motion below the knee and there is no sensation. He is extremely anxious, but suffers very little except from restlessness; his respiration is quite rapid—there are numerous fine moist râles over his chest; the heart has increased in frequency; his pulse is 120 to the minute, irregular in rhythm; the area of cardiac dulness is 14½ cm. from the median line, and the apex-beat is quite diffuse.

Discussion.—This case, followed more or less clearly for the past two years, affords you a clinical picture of the march of events and changes which occur at times in an individual with marked arteriosclerosis and atheromatous arteries, particularly where the pathologic process involves the coronary arteries. We see, first, symptoms that are referable purely to the myocardium, as evidenced by his symptoms during his first stay in the hospital; his attack of influenza and probably the strain of coughing at this time was just sufficient to produce a degree of cardiac dilatation to make him consult a physician; this, in turn, was soon followed by further dilatation of his heart from unusual exertion, and with this attacks of angina pectoris. An interesting feature of the anginal attacks is their frequency. It is quite unusual to see an individual have as many and as severe attacks as this patient presents. Then, lastly, as a result of his coronary sclerosis, he has had a thrombus form in his coronary artery which further damaged his myocardium, giving him the symptoms of which he now complains. Thrombi have also formed in his heart and he has had an embolus plug his right femoral artery.

Particularly do I wish to direct your attention to the symptoms of his coronary thrombosis:

First, the sudden onset of violent agonizing substernal pain which persisted constantly and continuously for several hours. This particular pain differs from the pain of ordinary angina in its duration.

Second, the sudden cessation of the pain; but with its cessation

there is marked evidence that the heart has been profoundly disturbed and badly injured.

Third, the evidence which makes us feel sure that such changes have occurred in the heart is that the thrombus formed within the left ventricle has been dislodged, or certainly a part of it has been dislodged, and has completely plugged the femoral artery just below Poupart's ligament.

It probably is not common to find a large superficial artery completely plugged as you see this today. When such changes do occur usually smaller vessels are affected, and those of the brain most often. Unfortunately, we have about reached our limit in treating this patient. About all that we can do for him at the present time is to keep him as comfortable as possible and wait for the end. The case is extremely difficult to handle because he belongs to that class of unfortunate individuals who cannot take morphin.

NOTE.—The patient lived two days after the clinic, dying very suddenly. At autopsy the interventricular branch of the left coronary artery was thrombosed about 4 cm. from its origin; an infarct 2.5 x 1.5 cm. was found involving the tip of the left and part of the right ventricles; intramural thrombi were found in both ventricles.

CLINIC OF DR. JOHN P. MUNROE

CHARLOTTE SANATORIUM, CHARLOTTE, NORTH CAROLINA

SEVERE HEADACHES

WE have presented a number of cases that are grouped together on the basis of their chief symptom—severe headache. Some of those presented have other symptoms perhaps as prominent as the headache, and are presented on account of the diagnostic difficulties found.

While one may not adhere strictly to any classification of the causes of headache, the ones usually given in text-books constitute a good working basis, which one may modify as he wishes.

The general classification of the causes of headache includes:[1]

1. Toxemias, exogenous and endogenous, in which impoverished or disordered blood is brought to the brain, as in (*a*) gastro-intestinal disorders; (*b*) diathetic states; gout, uremia, rheumatism, or the so-called indurative headaches; (*c*) infections; malaria, fevers, etc.
2. Toxic causes: lead, alcohol, tobacco, etc.
3. Neuropathic states: epilepsy, hysteria, neurasthenia.
4. Reflex causes: ocular, auditory, gastric, sexual.
5. Organic disease: tumors, syphilis, neuritis, meningitis, and diseases of the cranial bones.

Very frequently several causes act together.

Headaches connected with menstruation are difficult to place in this classification. They are probably both toxemic and reflex in most cases.

Most of us in studying a case first make a general examination, noting any sign or symptom that may throw light on the

[1] Dana: Text-book of Nervous Diseases.

investigation. We usually are gratified if we can find an organic cause, especially if it is one that can be removed. The existence of a toxemia should always be carefully considered. I believe the general practitioner attaches more importance to reflex causes than to any other. It is interesting to note that in Cabot's graphic representation of causes the psychoneuroses stand at the head of the list. He gives also a very long line to represent unknown causes. I quite agree with Cabot[1] and Thomas[2] in controverting the usual text-book statement that the headaches of elderly persons are frequently caused by arteriosclerosis. It is only when nephritis and high blood-pressure are present that headache in these cases may be expected. It is also interesting to note that eye-strain is considered a very important cause by the general practitioner. A large proportion of cases referred to me come through the oculist or are previously examined by him.

CASE I.—This is a woman thirty years of age, married, and has three children, the youngest child being five weeks of age at the time this patient entered the hospital, which was February 19, 1918.

Her chief complaint is recurring attacks of headache associated sometimes with what her husband describes as "fainting spells." Usually the headache follows the fainting spells and frequently vomiting also occurs.

The family history is negative.

Past History.—Patient has had two attacks of pneumonia, one twelve years ago, which was followed by severe earache. She has been practically deaf in the left ear ever since. One year ago had an operation for hemorrhoids and one ovary was removed. She has had three children, all normal deliveries and no miscarriages. She has had marked dysmenorrhea.

History of Present Illness.—The headache, which is now the chief symptom, has been present more or less for the past two and a half years. At first it recurred only once a month, but later became more frequent. Following her last delivery, which

[1]Differential Diagnosis, vol. i.
[2]Osler's Modern Medicine, vol. vii, p. 336.

was January 15, 1918, her right arm became powerless and remained so for about four days. At this time also her right eye became drawn inward. Since that time the so-called fainting attacks, followed by vomiting and severe headache, have recurred every few days, and she has been confined to the bed most of this time.

Physical Examination.—When first seen the patient was lying on her back with eyes partially closed, mouth partially open, and the jaw fixed. The arms and legs were rigid. She soon came out of this condition, began vomiting, and complained of severe pain in the head, more marked in the left parietal region. Her complexion was sallow and there was slight enlargement of the cervical glands. Several decayed teeth had been treated by a dentist, but some pyorrhea was still present. Heart, lungs, and abdomen negative. Knee-jerks slightly exaggerated, no clonus, no Babinski, pupils normal. The eye-grounds showed the beginning of a choked disk. The grasp of the left hand was slightly stronger than that of the right. Urinalysis was negative except for trace of albumin and trace of indican. White blood count 8700, blood Wassermann negative. Spinal puncture showed a marked increase in spinal fluid pressure and the Wassermann of same was negative and cell count negative.

We have here a group of symptoms that point rather distinctly toward a brain lesion of uncertain duration. The so-called fainting spells, on investigation, proved to be a form of convulsion with a tendency to opisthotonos. The history of earache, with subsequent deafness and recurring pain in the left side of her head, extending over a period of two and a half years, would suggest metastatic abscess. The fact that all the symptoms became exaggerated immediately after the last child's birth would suggest that something of an acute nature occurred at that time. The choked disk and increased intraspinal pressure indicated unmistakably increased intracranial pressure, but for some time there were no distinct localizing signs. It was interesting to note that after drawing off about 30 c.c. of spinal fluid all the symptoms were very much relieved. Formerly she

had been eating very little and vomited often. Now she began eating regularly, seemed to enjoy her meals, and digested them perfectly. At times there was slight internal strabismus of the right eye. Gradually, too, there developed a noticeable paresis of the right side of the face. Radiograph of the head showed an indistinct circular shadow in the left parietal region.

She had been under observation about two weeks in the hospital when she had another convulsion, which was the first to occur after the spinal puncture. Following this were the usual vomiting and headache and some definite localizing signs. There had been some slowness and hesitancy in speech from the beginning, and this now developed into a well-marked aphasia. Previously both knee-jerks had been slightly exaggerated. Now the right became markedly so, and slight clonus and Babinski appeared in the right. Again spinal puncture was used and the pressure was found to be somewhat above 260. As previously, all the symptoms were relieved by drawing off the spinal fluid, but the relief did not last so long as it did the first time. It was found at this time, too, that choked disk was more marked and vision was distinctly diminished.

Diagnosis.—Considering signs and symptoms presented, I had no hesitation in making a diagnosis of a brain tumor, located in the left parietal region. I advised an operation to be done, primarily to relieve the intracranial pressure and also to remove the tumor, if possible. I impressed upon the husband the seriousness of the situation and told him frankly that it was quite possible the growth was malignant, in which event an operation, at best, could give only temporary relief. It was natural that he should consider it for a considerable length of time before agreeing to an operation. The patient grew rapidly worse, however, and spinal punctures gave so little relief that they were discontinued. The convulsions became more frequent and so severe that ether was resorted to for control of them. In her waking moments the patient herself began begging for an operation.

On March 19th, although the patient was almost *in extremis*, Dr. (Captain) Scruggs operated in the left parietal

region. He removed a piece of bone about 1½ by 2 inches. As soon as the dura mater was opened an oval vascular tumor was found, measuring about 1 inch long by ½ inch on the surface. The tumor was so vascular and the patient's circulation had become so weak that no effort was made to remove it. The wound was closed up in the usual way and for several hours the patient lay in a dead stupor. Within twenty-four hours she was sufficiently aroused to take a little nourishment, but could not speak. Her right leg and right arm were completely paralyzed. From this time on she gradually improved, had no more convulsions, and did not complain of headache. On April 6th she was dismissed from the hospital and taken to her country home, a guarded prognosis being given. At this time, June 12th, her speech is still markedly deficient, but she has had no convulsions, but little pain in her head, and is able to attend to some of her household duties. They are now asking about the second operation, which was spoken of at the time the decompression was done. It is proper to say that under the circumstances one could not say definitely what kind of tumor it was. It appeared to be a glioma, but it was too vascular for even a small section to be taken for examination.

CASE II.—Man aged thirty-three years, married, and is a farmer. His chief complaint is severe headache, originating behind the right ear and extending over the vertex.

Family History.—One sister at the age of ten became paralyzed and died after a short illness. One brother at unknown age died of some "meningeal trouble."

Past History.—Patient denies any luetic history, but his family physician tells me that about ten years ago he treated a local sore, which he diagnosed chancroid. He did not give him any constitutional treatment. It is significant, however, that about eight years ago he went to Hot Springs, Arkansas, and presumably took the mixed treatment.

Present Illness.—For five or six years he has been suffering with a dull headache. During the past winter the pain in the head had become so severe that his physician frequently gave him morphin for relief. Occasionally he had so-called rheu-

matic pains in one knee. The headache has been most severe in the afternoon and evening.

Physical Examination.—The patient is a stout, well-nourished man, with facial expression that indicates suffering or worry. The tongue is clean, the throat normal, and there are a few decayed teeth. Lungs and heart negative. Knee-jerks exaggerated, no clonus, no Babinski. Pupils react sluggishly to light. The right pupil is dilated. The patient says his pupil has been dilated for four or five years. The eye-grounds are normal. Urinalysis negative except that some albumin is present. White blood count 8200. Blood Wassermann positive.

Diagnosis.—Cerebral syphilis, with the lesions most marked at the base of the brain on the right side posteriorly. There is doubtless a periostitis with a meningitis that has involved some of the fibers of the right oculomotor nerve.

Treatment.—Salvarsan intravenously was begun January 25th, and given regularly once a week until five doses were given. He was then given mercury and the iodids. His family physician was requested to give him mercury hypodermically for a period of five weeks. On account of the appearance of salivation this program was not carried out. He returned to me May 29th very much discouraged and suffering again almost as much as formerly. His headache was gradually relieved under the first course of salvarsan treatment, and had entirely disappeared before the fifth dose was given.

In beginning the treatment again I was convinced that the intraspinous treatment should be used as well as the intravenous. On May 29th I gave him 0.4 gm. intravenously, and the next day gave him intraspinously salvarsanized serum to which was added 0.3 mg. of salvarsan. A week later I gave him another dose intravenously, but did not follow it with the intraspinous because his back was still somewhat sore. Today we are giving him another dose intravenously and tomorrow will repeat the intraspinous treatment. He is more encouraged about himself today than usual and says he has not felt so well in years. The spinal fluid was not examined until May 30th, at which time the cell count was 540. This convinces me more than

ever that to effect a cure we must continue the intraspinous treatments.

Our pathologist has just reported the spinal fluid cell count is today reduced to 90.

CASE III.—Woman aged forty-six, married; separated from husband. First examined March 16, 1918. This patient presents symptoms very similar to Case II.

Family history negative.

Past History.—Negative, except that seventeen years ago had a growth removed from the right knee, said to have been sarcoma.

Present Illness.—In the summer of 1916 she began having dull pain in the left temporal region. For the last ten weeks the pain has shifted and has been very severe in the left occipital region. Three weeks before her examination complete ptosis developed in the left eyelid, and along with this a constant pain behind the left eye. This pain behind the eye and in the left occipital region has been so severe that her physician has been forced to give her an opiate in some form or other. At present she is taking a teaspoonful of papain several times a day.

Physical Examination.—Teeth and throat in good condition, heart and lungs negative. Knee-jerks slightly exaggerated, the right more than the left. Eye-grounds normal. Right pupil normal. Left pupil dilated and complete ptosis of left eyelid. Left eye stationary, directed upward and outward. Urinalysis negative except for a trace of albumin. White blood count 8200. Blood-pressure 160 S. and 100 D. Blood Wassermann negative. Spinal fluid no increase of pressure, Wassermann negative, and cell count 12.

Diagnosis.—This is a case that presents considerable difficulty in diagnosing. The severe headache localized on one side and the complete paralysis of the third nerve on the same side with an exaggeration of the knee-jerks, especially the right, point to a lesion of some kind at the base of the brain on the left side. The absence of choked disk and the normal spinal fluid pressure argue against a brain tumor. The severe headache, somewhat paroxysmal in character, being worse late in the evening,

and the selective action on one of the cranial nerves, point to luetic infection. Against this is the negative Wassermann, both of the blood and the spinal fluid, and negative clinical history, so far as can be ascertained. Another point in favor of luetic infection is the cell count in the spinal fluid, which is 12, considerably above normal. Under the circumstances I felt justified in making a tentative diagnosis of cerebral syphilis, and expected to get further light by the therapeutic test.

Treatment.—Beginning March 28th I gave her a moderate dose of salvarsan, 0.3 to 0.4 gm., once a week for eight weeks. I was delighted to find that after she had received three doses the headache was very much relieved and, after the use of six doses, she needed no opiate or medicine of any kind for relieving the headache. The last dose was given May 18th, and on May 20th she was able to open the left eye and now appears to be almost normal. This would indicate that the diagnosis of luetic infection is correct. Having completed the first course of salvarsan, we will keep her under observation for a limited period of time, and then advise that one or more courses be given, until all symptoms have disappeared and until the cell count in the spinal fluid becomes normal, regardless of the Wassermann test.

CASE IV.—Male, unmarried; machinist, aged thirty-four.

Family history negative.

Past History.—Three years ago he suffered considerably with asthma. This continued until about four months ago, when he had a growth removed from the nose, the nature of which is unknown.

Present Illness.—For one year has had severe headache, especially marked in occipital region. Has had frequent weak spells, during which he falls and sometimes becomes unconscious for a few minutes. So far as known he has never had any convulsions. For the last four months his eyesight has been gradually failing. I was called to see this case in consultation with Dr. Otho B. Ross, the family physician, and with him I made my first examination February 24, 1918.

Physical Examination.—Briefly, the signs presented were as follows: the pupils react to light and accommodation, partial

paralysis of the sixth and seventh nerves on the right side, with slight strabismus and occasional double vision. Slight loss of sensation in both arms and hands. Knee-jerks absent. No clonus, no Babinski. Eye-grounds show choked disk, and examinations made later showed that it was increasing slowly. Radiograph of head negative. Urinalysis showed a few hyaline and granular casts, otherwise negative. Blood Wassermann negative. Spinal fluid Wassermann negative, pressure normal, and cell count normal.

Diagnosis.—The symptoms and signs point very strongly to a brain lesion. The interesting question is, What is its nature and where is it located? There is nothing in the clinical history nor in the laboratory test to indicate luetic infection. This may be further eliminated by the fact that the family physician had given him a specific treatment, to a limited degree, it is true, but without producing the slightest effect upon the symptoms. The question of brain tumor is strongly suggested by the choked disk, severe headache, dizziness, and occasional attacks of unconsciousness. It will be noticed that the sixth and seventh nerves are involved on both sides. This fact and the absence of knee-jerks point very strongly to a cerebellopontine tumor. The question has been raised, If there is a brain tumor, why is there no increase in the spinal fluid pressure? The answer is that the tumor in this region would probably close the aqueduct of Sylvius. This would be accompanied by increase of pressure inside of the cranium and in the ventricles, but not in the spinal cavity. After following this case with Dr. Ross for two months and finding that the symptoms were increasing slowly, it is true, I advised an operation for decompression. Perhaps a surgeon especially skilled in brain surgery would operate over the supposed seat of the tumor. In this case Dr. Gibbon, the surgeon called in, with Dr. Ross and myself, thought a simple decompression in the temporoparietal region was the operation of choice. This would save the eye temporarily at least. If the growth should be a malignant one, no operation would be of permanent benefit. It is claimed by some that a decompression sometimes gives permanent relief, especially if the growth is of a

tubercular nature, as this kind of growth is apt to reach its maximum size, then discontinue growing, and perhaps atrophy. After considerable hesitation the patient finally agreed to an operation, for the pain was becoming unbearable and the eyesight continuing to grow worse.

Some time later Dr. Gibbon did a simple decompression in the right parietotemporal region. Patient made an uneventful recovery and for a while was very much relieved. His eyesight became better, his walking more steady, and for a while there was no headache. Later on symptoms of pressure gradually returned and today he is suffering as much as ever. He can scarcely walk, headache is severe, vision bad, and choked disk more pronounced than ever. Another decompression on the opposite side with a view to taking out a larger piece of bone than formerly is under consideration. At best, however, the outlook is unfavorable.

CASE V.—Female, unmarried, aged twenty-two years.

Family history negative.

Past History.—Six years ago had an acute attack of what was called "nephritis." Six months ago had whooping-cough, followed by otitis media. She seems to have recovered entirely from the ear trouble. Most of her life she has been subject to attacks of headache, and for the past two months it has been very severe and almost constant.

Present Illness.—She was referred to me on account of her severe headache, general nervousness, and frequent micturition. She is an intelligent young woman, well educated, and has a tendency to introspection. Appetite poor, digestion fair, bowels constipated, menstruation regular and normal.

Urinalysis negative except large amount of indican present. White blood count 13,200, blood Wassermann negative.

Physical Examination.—General appearance, well nourished and complexion good. Tongue clean, three decayed teeth have been filled, one of them having had the nerve destroyed. None of the wisdom teeth have erupted. Throat in good condition. Heart and lungs negative. Pupil reflexes normal, knee-jerks weak. Cystoscopic examination of the bladder (by Dr. Crow-

ell) showed a congested mucous membrane. Radiograph of the teeth showed infection around the root of one tooth which had been filled, and all of the wisdom teeth leaning against the adjacent molars in a direction that would appear to make it difficult for them to become erupted. She was wearing glasses for hyperopia +.75 D. S. An examination by Dr. Peeler showed a high degree of astigmatism.

Diagnosis.—Here is a case in which there does not seem to be any organic lesion of the brain or nerves. Neither my examination nor that of Dr. Crowell reveals anything seriously wrong with the kidneys or bladder. Her chief symptoms, namely, headache and frequent micturition, are probably due in part to toxemia resulting from constipation and the absorption of toxins from the lower bowels. The excess of indican and the moderate leukocytosis may both be partly dependent upon this. An infected tooth is also to be taken into account in this connection. Perhaps more important still are the reflex causes connected with the astigmatism and the impacted teeth.

Treatment.—I adopted treatment with the view to remedying the factors above outlined. After adopting the usual remedies, chiefly dietetic, for correcting the intestinal indigestion, I referred her to a dentist (Dr. Hoffman). He cleaned out the root of the infected tooth and refilled it. The wisdom tooth that was worst impacted he extracted. I had the oculist fit suitable glasses for the astigmatism. After these various things had been attended to relief was almost immediate, both from the headache and the frequent micturition. This was more than a month ago and she is still doing nicely. I am keeping her under observation, and realize that it is quite probable some of the other impacted teeth may have to be removed.

CASE VI.—Man, unmarried, aged eighteen years.

Family history negative.

Past History.—Negative except that three years before my first examination, which was August 5, 1917, he had a fall from a wagon, striking his head rather hard on the ground. It was two months after this that he began having the "spells" for which he consulted me. He denies luetic infection.

Present Illness.—In September, 1914, he had an attack of dizziness and unconsciousness, followed by severe headache. These attacks have recurred at irregular intervals ever since, sometimes one month, sometimes several months intervening. The headache sometimes precedes but more often follows the unconscious periods, and they usually come on in the morning. During the last few months they have become rather more frequent, and sometimes a distinct convulsion develops.

Physical Examination.—He is comparatively well nourished, but there is slight atrophy of the right leg and arm. His face presented a rather dull expression, voice somewhat thick, and gait slightly spastic on the right side. A pustular eruption was pretty general over the body and most marked on the back. Tongue heavily coated, pyorrhea quite extensive, but no teeth badly decayed. Nose and throat in good condition. Lungs negative, heart presented a loud systolic murmur at the base, transmitted into the neck, a distinct thrill being felt over the same area. Blood-pressure 105 S. and 80 D. Pupil reflexes normal. Eyegrounds normal. Right knee-jerk exaggerated, left knee-jerk weak. Urinalysis negative. Blood Wassermann negative, white blood count 7000.

Diagnosis.—Here is a situation where we have been handicapped by two difficulties. One is the vague and indefinite history which was gotten chiefly from the patient himself. The other is the fact that for a long time it was difficult to keep the patient here long enough to make a thorough examination. He lives in a distant town and usually insisted on going back home the afternoon of the same day that he came to my office. The fact is that, although I saw him first in August, 1917, it was not until April, 1918, that I persuaded him to stay in the hospital long enough for a real study of his case. The facial expression, the unilateral spastic gait, and the exaggerated knee-jerks on the same side point to an organic lesion on the left side of the brain. The history of the attacks coming on soon after a fall on the head points to a traumatism of the brain. A hemorrhage with a subsequent development of a cyst around the clot is a possibility. While the symptoms of irritation have increased

perceptibly within the last few months, one would scarcely be justified in diagnosing a growing tumor or cyst. There has been no choked disk. I did not have an opportunity of doing a spinal puncture until April 4, 1918. This showed no increase of pressure, Wassermann negative, cell count 6. While the history, as obtained, points to traumatism, and while the blood test and spinal fluid findings indicate no specific infection, the physical examination is so suggestive of syphilis of the brain that I felt justified in giving him the benefit of therapeutic test. I began the use of salvarsan April 4th and gave him a small dose once a week for eight weeks. The results confirm the diagnosis of cerebral syphilis. He looks like a different man, walks with a sprightly step, and has had no convulsions or headache of any consequence since the treatment was begun.

CASE VII.—Male, married, aged fifty-six years; minister.

Family History.—Negative except that father died of apoplexy at an advanced age.

Past History.—He has had no serious illness, but has led a very strenuous life as preacher and pastor. For many years has had occasional attacks of headache, which were thought to be due to eye-strain and errors of refraction. About eighteen months ago insomnia was added to the headache, and it was found that he had a blood-pressure of more than 200. He underwent treatment for several weeks in New York City, and later went to Hot Springs, Virginia, where he took the baths. His symptoms were so far relieved that he resumed his strenuous work as pastor one year ago, continuing until about two months ago, when he first consulted me.

Present Illness.—His chief symptoms I found were severe headache, pressure on top of the head, insomnia, occasional nausea, but no vomiting. Appetite good, digestion fair, bowels kept open by daily doses of sal hepatica. He complained of frequent accumulation of gas.

Physical Examination.—His general appearance is that of a well-nourished man with a troubled, anxious expression. Tongue is slightly coated, teeth in good condition, several have good fillings. More than a year ago radiographs were

made of the teeth, two, having abscesses, were extracted and the rest have been under the constant care of an expert dentist. Lungs are negative. The heart is considerably enlarged and there is sharp accentuation of the second aortic sound. Blood-pressure 240 S. and 140 D. Pupil reflexes normal, knee-jerks slightly exaggerated. Urinalysis sp. gr. 1018, albumin present in large quantity, sugar negative, bile negative, indican excessive, many hyaline and granular casts and epithelial cells. White blood count 10,000. Wassermann negative.

Diagnosis.—With the above history, signs, and symptoms one would have little difficulty in making a diagnosis of chronic nephritis. The patient's circumstances were such that he could not remain in the hospital for treatment at the time of the first examination. He promised to go home, however, arrange his affairs, and return as soon as possible.

When he entered the hospital five weeks ago practically the same conditions existed as already described. The urinary output by the red test was about 60 per cent. of normal. With rest in bed, milk diet, sweat baths, and elimination by the bowels his headache and insomnia have been largely relieved. The blood-pressure has been reduced very little.

Prognosis and Discussion.—The outlook is serious, and my experience is that one in this condition seldom lives one year; more often it is a matter of a few months. The surprising thing is that, although he has been under the care of several most excellent physicians, the serious aspects of this case were either not recognized or not taken firmly in hand until too late for any treatment to be of much avail. A persistent headache with high blood-pressure always calls for thorough investigation with reference to the kidneys. In this case, as in many that I have seen, undue attention seems to have been directed to his eyes and errors of refraction.

Proper and intelligent care was given to his teeth. Even granting that a thorough investigation of the kidneys would not have disclosed any organic change eighteen months ago, still the conditions, as outlined, were so suggestive that he should have had repeated examinations and careful oversight all the time.

It was a serious mistake to allow him for nearly a year to continue in the full work of a pastorate where the duties were known to be large and exacting.

CASE VIII.—Man, aged twenty-nine, unmarried. Mill operative. This patient was first seen seventeen days ago, and his chief symptom was severe pain in the left parietal region.

Family history negative.

Past history negative.

Present Illness.—He dates his illness from April 1, 1918, when he had a very severe case of influenza. Following this an otitis media developed in the left ear. The membrane ruptured and the pain disappeared, a tolerably profuse discharge resulting. Ten days later he had severe pain in the left parietal region. He was in Indianapolis at that time and fell into the hands of a competent surgeon. He made a diagnosis of "abscess of the brain" and advised an operation. This the patient refused. Later his friends brought him back to his North Carolina home and sent him to me for examination.

I found him still suffering with severe pain over the left side of the head, marked hebetude, slowness of speech, and evidence of beginning aphasia.

Physical Examination.—Pale, somewhat emaciated, tongue clean, pupillary reflexes normal, teeth carious, no enlargement of cervical glands. The arm-jerks were normal, knee-jerks weak, co-ordination good, no Romberg, no clonus, no Babinski. Heart and lungs negative. Hearing good and equal in both ears, both cords normal, no choked disk (Dr. Peeler). Urinalysis faint trace of albumin, trace of indican. White blood count 11,200. Blood Wassermann negative. Patient was advised to come to hospital as soon as possible for further examination and probable operation. He entered the hospital one week ago and the symptoms of brain pressure had increased considerably since the first examination. His headache was more severe and his mental condition almost stuporous. He complained of not seeing well and often seeing double. Right knee-jerk exaggerated, clonus and Babinski also present in the right. Left knee-jerk slightly exaggerated, slight clonus, no Babinski.

During this second examination a spinal puncture was made and there was slight increase of pressure, Wassermann negative, cell count 10 polymorphonuclear, 2 mononuclear (Dr. Barret).

Radiograph (Dr. Lafferty).—"The transverse view shows very much clouding around the mastoid cells on the left side and the auditory canal is larger than normal, as if some of the bone had been removed. The mastoid cells are practically obliterated and the dense area extends upward much higher than normal. Just above this region is a translucent area that may be a cyst or abscess, although it does not seem to have clearly defined walls. The sella turcica is also abnormal and it seems as if it were filled with some dense material that projects forward."

Diagnosis.—The history of this case clearly indicates that the beginning of this trouble is to be found in the influenza and the middle-ear disease, occurring about the first of April. Although there is no special tenderness about the mastoid cells, the *x*-ray examination indicates disease there which may call for operative treatment later. There is evidently a lesion in the left parieto-temporal region involving the speech center. It would appear also that there is some lesion at the base of the brain involving the sella turcica.

The diagnosis made in Indianapolis was "abscess of the brain above the ear." The history of the case would exclude acute abscess, but it may very reasonably be a chronic abscess. The *x*-ray examination suggests a cyst. This is quite possible as a result of a hemorrhagic encephalitis, resulting from a non-suppurative infection from influenza or otitis media. In either event it appears that there is a diseased condition both at the cortex of the left side and at the sella turcica. The cortical lesion is now demanding immediate operation, so at my request Dr. Scruggs operates today. We are expecting to find either a chronic abscess or a cyst developed upon a hemorrhagic encephalitis.

Operation.—After making the usual incision, Dr. Scruggs removed an oval-shaped piece of bone about 1¼ inches in its longest diameter. The membrane immediately bulged out into the opening. A crucial incision was made in the dura and a cyst

was disclosed about the size of a large plum. The cyst was opened and its contents discharged, but the area was too vascular to justify any attempt at removing the cyst wall.

Prognosis.—This operation should give at least temporary and possibly permanent relief, so far as the cortical lesion is concerned. As there appears to be a lesion at the sella turcica, it is quite possible that serious trouble may result from it later on.

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